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Clinical impact of supraventricular tachycardias in patients with pulmonary hypertension
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Purpose: Supraventricular tachycardias (SVT) are frequently observed in patients with pulmonary hypertension (PH). Their prevalence and impact on prognosis of patients are not known.

Methods: We retrospectively studied the prevalence of SVT and survival in 998 patients with PH (aged 59±16 years; 451 males).

Results: SVT was observed in 234 (23%) patients. Atrial fibrillation (AF) was the most prevalent (n=168), followed by atrial flutter (AFL) (n=52), other atrial tachycardias (AT) (n=18), and AV nodal re-entrant tachycardia (AVNRT) (n=3). Prevalence of SVT in main PH classes is shown in Table. Excessive prevalence of SVT was observed in patients with PH associated with congenital heart disease (p<0.05). Other differences did not reach significance. Patients with permanent SVT were in higher NYHA functional class compared to the rest of population (3.2±0.9 vs. 2.7±1.3; p=0.05). Total of 416 (42%) patients died during mean follow-up of 8.7±5.1 years. Presence of any type of SVT was not associated with the mortality.

Conclusions: Patients with PH had high prevalence of SVTs. Permanent SVTs were associated with worsening of functional class. Occurrence of atrial arrhythmias had no mortality impact in total PH population.

916 | BEDSIDE
Current era survival in patients with pediatric pulmonary arterial hypertension
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Background: Pulmonary arterial hypertension (PAH) is a rare disease characterized by a progressive increase of pulmonary vascular resistance leading to right ventricular failure and premature death. Epidemiological data are scarce, particularly in the pediatric population. Objectives: the aim of the present study was to assess prospectively the current era survival of pediatric PAH patients (P-P AH) and to compare it with the survival of adult PAH (A-P AH) patients with similar etiologies.

Methods: We included in the study consecutive PAH patients aged ≤18 years (Adult) referred to a single center from February 1992 to October 2013. Due to the epidemiology of pediatric PAH disease (n=65) 22 (34%) 6 (9%) 0 3 (4.5%) 33 (51%)

Conclusion: We retrospectively studied the prevalence of SVT and survival in 998 patients with PH (aged 59±16 years; 451 males).

Results: SVT was observed in 234 (23%) patients. Atrial fibrillation (AF) was the most prevalent (n=168), followed by atrial flutter (AFL) (n=52), other atrial tachycardias (AT) (n=18), and AV nodal re-entrant tachycardia (AVNRT) (n=3). Prevalence of SVT in main PH classes is shown in Table. Excessive prevalence of SVT was observed in patients with PH associated with congenital heart disease (p<0.05). Other differences did not reach significance. Patients with permanent SVT were in higher NYHA functional class compared to the rest of population (3.2±0.9 vs. 2.7±1.3; p=0.05). Total of 416 (42%) patients died during mean follow-up of 8.7±5.1 years. Presence of any type of SVT was not associated with the mortality.

Conclusions: Patients with PH had high prevalence of SVTs. Permanent SVTs were associated with worsening of functional class. Occurrence of atrial arrhythmias had no mortality impact in total PH population.
Conclusion: The 6-MWD is an independent predictor of prognosis in paediatric PAH, that reflects disease severity and clinically relevant exercise-tolerance and therefore qualifies as a treatment target. A large decrease in tsCO2 during 6-MWT, adjusted for the presence of a shunt, indicates an additional risk factor for worse prognosis in children with PAH.  

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Increase in tricuspid regurgitation severity impairs outcome in patients with pulmonary hypertension  
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Purpose: Patients with pulmonary hypertension (PH) often present with tricuspid valve regurgitation (TR). We aimed (1) to establish the impact of increasing TR severity and (2) to evaluate impact of new significant TR on outcome in patients with PH.  

Methods: Files from patients included in the institutional PH database between July 1989 and August 2012 were reviewed. Patients were stratified into patients with mild TR(<2/4) and significant TR(≥2/4) but didn't differ significantly from patients with significant TR at first presentation.  

Results: Data were available for 653 patients, 64% female, aged 60 yrs ± 15. Pulmonary hypertension was idiopathic PAH in 37.8% of patients, due to left heart disease in 20.2%, due to lung disease in 5.2%, and of unclear origin in 3.4%. During a mean follow-up time of 4.2 years, 256 occurred events. Multivariable analysis including also gender, mean PAP, PCW, RA pressure, TR severity and TAPSE to be related to worse outcome. Multivariable analysis with age (p≤0.001; HR=1.036 (1.019-1.054)) and TR severity (p=0.010; HR=1.466 (1.097-1.960)) as independent predictors of worse outcome (Fig. 1A). We subsequently developed significant TR, outcome was impaired compared to patients with TR <2/4 but did not differ significantly from patients with significant TR at first presentation.  

Conclusions: TR severity is independently related to worse outcome in patients with a pressure-loaded ventricle. Furthermore, survival is impaired if patients develop significant TR during follow-up. The development of significant TR should alert for possible disease progression.  

920 | BEDSIDE  
Right ventricular echocardiographic indices predict high altitude pulmonary pressure increment in lowlanders  
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Background: The determinants of high altitude pulmonary edema (HAPE) remain ill defined. Increased hypoxia-related pulmonary artery pressure (PAP) is recognized as a key component. No validated parameter exists to predict the development of HAPE in recreational climbers. We aimed to assess whether baseline right ventricular (RV) echocardiographic indices were predictive of an increased hypoxic PAP response.  

Methods: 14 lowlander subjects (8 men; ages 27-65) were assessed by echocardiography at sea level (Montreal), 3450m (Namche Bazaar) and 4730m (Chukking) during an expedition Nepal. Baseline RV performance parameters were compared to the systolic PAP (sPAP) at high altitude; correlation coefficient (r) and coefficient of determination (r2) were calculated.  

Results: At high altitude, none of the subjects had clinical criteria for HAPE, although all except one had ultrasonic signs of interstitial lung water. sPAP increased in all between Montreal and Chukking (mean PAP 27.4±5.4 mmHg vs. 39.3±7.7 mmHg respectively; p<0.001). Sea level RV Tei index by tissue Doppler was moderately correlated to the sPAP increment (r2=0.37), as was the S velocity (r2=0.27). Baseline TAPSE strongly correlated with the sPAP increment (Fig. 1). RV longitudinal strain baseline value did not correlate with sPAP increment (r2=0.05), but strain increment between Montreal and Chukking was moderately correlated to the sPAP reached at the 4730m (r2=0.39).  

Conclusions: RV TAPSE, S' and Tei index at sea level correlate with the sPAP amplitude induced increment in lowlanders. These findings reinforce the role of RV function in the development of HAPE and, should they be confirmed on a larger population, suggest that these indices could help counsel lowlanders before attempting high-altitude climbs.  

921 | BEDSIDE  
Pulmonary artery occlusion waveform analysis for the assessment of pulmonary vascular disease in pulmonary hypertension due to left heart disease  
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Purpose: Pulmonary hypertension (PH) due to left heart disease (LHD) is the most common subset of PH. It is defined by an increase of mean pulmonary artery pressure (mPAP) ≥25mmHg in the presence of a mean pulmonary arterial wedge pressure (mPAWP) ≥15mmHg. In the 5th World Symposium on Pulmonary Hypertension in Nice, PH due to LHD (post-capillary PH) was subdivided into two hemodynamic phenotypes, "isolated" post-capillary PH (IPCH, diastolic pulmonary vascular pressure gradient (DPG) <7mmHg) and "combined" pre-capillary and post-capillary PH (CPCHP, DPG ≥7mmHg). Recent data have shown that patients with post-capillary PH and a DPG ≥7mmHg have an increased mortality and significant pulmonary vascular disease. Pulmonary artery occlusion technique assesses the decay from pulmonary artery pressure to PAWP to approximate the pressure in pre-capillary small pulmonary arteries (POCCL). With POCCL, pulmonary vascular resistance can be partitioned into larger arterial (upstream, Rup%) and small arterial plus venous (downstream) components. The aim of the present study was to assess the accuracy of pulmonary artery occlusion waveform analysis (PAOWA) in patients with CPCHP.  

Methods: PAOWA was performed in 37 patients undergoing right and left heart catheterizations at rest and after inhalation of 40ppm nitric oxide (NO). 10 patients were classified as IPCPH with a transpulmonary gradient >12mmHg, 20 as CPCHP and 7 as idiopathic pulmonary artery hypertension (iPAP).  

Results: The lowest Rup% was observed in patients with iPAP (67.1±12.1%) and CPCHP (74.5±13.7%; p=0.57), while patients with IPCPH showed higher Rup% (94.5±5.3%). While iPAP patients (0.52±11.5, p=0.91) did not show a change in Rup% upon NO, an increase in Rup% could be observed in patients with CPCHP (6.6±7.35%, p=0.054). A significant correlation between DPG and Rup% was observed (r=0.41; p=0.011).  

Conclusions: PAOWA confirms that patients with PH due to LHD and a DPG >7mmHg (CPCHP) have pulmonary vascular disease similar to iPAP, whereas the Rup% was lower than in iPAP patients and increased upon NO, which might be due to reactive vasoconstriction in this condition.  

922 | BEDSIDE  
Epidemiology of combined pre-and post-capillary pulmonary hypertension in patients with heart failure  
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Purpose: Heart failure (HF) is an increasingly important cause of morbidity and mortality. Right ventricular (RV) function and the presence of pulmonary hypertension (PH) have been shown to be of prognostic relevance in HF. In the 5th World Symposium on PH on PH in Nice, PH due to left heart disease (post-capillary PH) was subdivided into two phenotypes, “isolated” post-capillary PH (iPAP, diastolic pulmonary vascular pressure gradient (DPG) ≥7mmHg) and “combined” pre- and post-capillary PH (CPCHP, DPG ≥7mmHg). Recent data have shown that patients with post-capillary PH and a DPG ≥7mmHg have an increased mortality and significant pulmonary vascular disease. We sought to study epidemiology, RV function and non-invasive predictors of CPCHP in HF.  

Methods: A retrospective data set of 3107 all-comers undergoing first diagnostic right and left heart catheterizations at rest was analyzed. 1063 patients were identified with having HF (664 patients with systolic heart failure [SHF]) and 399 with diastolic heart failure [DHF]). A prospective sample of 800 consecutive patients, comprising 391 patients with HF (172 patients with SHF and 219 patients with DHF), was utilized to validate the results of the retrospective data set.
Results: In the retrospective data set CPPCH was observed in 80 patients with SHF (12%) and 49 patients with DHF (12%). Similar results were found in the prospective database showing CPPCH in 24 patients with SHF (14%) and 26 patients with DHF (12%). Right to left ventricular ratio on echocardiography was higher in patients with CPPCH in DHF (r=0.15) compared to those with SHF (r=0.01, p=0.001). Multivariate analysis revealed COPD (p=0.003, Odds ratio: 4.111 [1.135:14.896] as an independent risk factor for CPPCH in SHF. In contrast, VHD (p=0.013; Odds ratio: 5.877 [1.463:23.610]) and tricuspid regurgitation jet velocity (p=0.012; Odds ratio: 3.449 [1.317:9.028]) were predictive for CPPCH in SHF.

Conclusion: The data indicate that patients with CPPCH in DHF show more signs of right ventricular overload than those with CPPCH in SHF. Mechanisms of increased RV afterload may differ in DHF versus SHF.

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Correlation between the severity of pulmonary hypertension and vascular remodeling in chronic obstructive pulmonary disease and diffuse parenchymal lung disease awaiting lung transplantation
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Purpose: Pulmonary hypertension (PH) is well recognized complication of chronic obstructive pulmonary disease (COPD) and diffuse parenchymal lung disease (DPLD). Local pulmonary arterial stiffness indexes correlated with hemodynamic severity in idiopathic PAH (IPAH). We analyzed the relation between the severity of PH and vascular remodeling in COPD and DPLD awaiting lung transplantation (LTx).

Methods: We studied 134 patients (p), 106 pre-LTx, NYHA 3-4, 41 COPD (58 ± 9 years, 9 females), 65 DPLD (60 ± 7 years, 19 females), 18 IPAH (51 ± 16 years, 11 females), and 10 healthy controls (51 ± 1.8 years, 6 females). All patients were submitted to left and right heart catheterization, and intravascular ultrasound (IVUS) in medium sized pulmonary arteries (PAs). We assessed the mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), aortic pressure, cardiac index (CI), pulmonary vascular resistance (PVR), and capacitance (Cp), time constant (tau: PVR/Cp), R-C relation, and local pulmonary arterial elastic modulus (EM: diastolic lumen area x pulse pressure/(systolic-diastolic lumen area)). We discarded p with PCWP >15 mm Hg.

Results: 48% (15/31) and 43% (25/58) of COPD p and DPLD p had precapillary PH, respectively. Both, CI (p<0.006) and PVR (p<0.043) were significantly correlated with EM in COPD. On the contrary, in DPLD p, only PVR correlated with EM (r=0.38), DPLD p showed higher EM beyond mPAP, associated with a downward shift of the R-C relationship.

Conclusions: The hemodynamic severity was correlated with vascular remodeling in pre-LTx COPD p. This was associated with a more preserved Cp and tau. DPLD p showed a worse vascular remodeling with lower tau and downward shift of the R-C relationship.

924 | BEDSIDE
Optical coherence tomography evaluation of pulmonary arterial vasculopathy in patients with systemic sclerosis
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Purpose: Our understanding of the pathophysiology of pulmonary vascular disease is incomplete as smaller pulmonary vessels are difficult to access in vivo. There has been no description of in vivo data about pulmonary vasculature of patients with Systemic Sclerosis (SSc) with and without PAH (pulmonary arterial hypertension). We used optical coherence tomography (OCT) to depict pulmonary arteries of less than 2mm in diameter during right heart catheterization (RHC).

Methods: In this ongoing study 18 stable SSc-patients with and without PAH underwent OCT of the pulmonary arteries. 14 patients met criteria for PAH (mean pulmonary artery pressure (PAM) at diagnosis 45 ±12.6 mmHg); 4 patients had no diagnosis for PAH (RHC). OCT was performed using a LightLab imaging wire with an outer diameter of 470 μm. After delivery balloon was wedged and the distal vessel filled with a 50/50 contrast saline mixture during pullback. Results: We obtained 82 runs in total, 4.5 mean per patient. 36 runs were not analysed due to vessel size >2mm (23 runs) and artefacts (13 runs). We were able to image pulmonary arteries <2mm in diameter in 17 out of 18 patients. The ratio of Intima media thickness area (IMT:A) as compared to total vessel wall area was highly significantly increased in the PAH group at the level of 2 mm vessels (29.5 ±6.8% vs. 21.1 ±1%, p=0.001) but not significant at 1.5mm vessel level (30 ±8% vs. 26 ±8.9%), IMTA correlated significantly with PAH at diagnosis (p=0.022). 8 runs of 10 SSC-PAH patients and 3 controls were screened for side branches <300 μm. In 4 SSS-PAH patients in whom afterload fell dramatically with therapy (PVR reduction >50%) we found a significant higher number of small side branches per cm vessel (5.8 ± 1.7 ±8, p=0.015). In the whole patient group the number of side branches did not correlate with PVR, PAM or time from diagnosis. 3 patients among the PAH group (25%) showed evidence of thrombus, recanalised clots or webs which was not previously diagnosed with VC scan or OA.

Conclusion: In this first series using OCT in pulmonary arteries of patients with SSC we found significant thickening of the IMT in moderate sized pulmonary arteries in patients with PAH compared to patients without PAH. Thickening was significantly associated with mean pulmonary artery pressures at diagnosis. Furthermore, the number of small side branches was significantly higher in patients who have reduced their PVR by >50% with therapy. The number of side branches might therefore predict better prognosis in PAH.

CARDIAC MAGNETIC RESONANCE T1 MAPPING: NOVEL AND IMPORTANT

933 | BEDSIDE
Myocardial biopsy for the validation of cardiac magnetic resonance T1 mapping for quantification of extracellular matrix

Background: Diffuse myocardial fibrosis / extracellular matrix expansion is a landmark feature of various cardiac diseases and is associated with an unfavorable prognosis. Recently, cardiac magnetic resonance (CMR) T1-mapping has been proposed for the quantification of extracellular matrix.

Purpose: This series mainly underlines 2nd important evidence: 1. Modified Look-Locker Inversion recovery (MOLLI) T1 mapping, allowing the calculation of extracellular volume (ECV). 2. Post-contrast multiple breath hold T1 mapping. In addition, native (pre-contrast) T1 mapping has gained increasing interest. Although CMR T1 mapping is a very promising technique and has been advertised as the new “non-invasive myocardial biopsy”, validation data, particularly in heart failure patients, are sparse.

Methods: 22 heart failure patients underwent CMR T1 mapping on a 1.5-T scanner and left ventricular biopsy within 4 weeks. The population consisted of 16 HFpEF (heart failure with preserved ejection fraction) patients, 3 patients suffering from dilated cardiomyopathy and 3 amyloidosis patients. In all patients the T1 mapping sequences were applied. Left ventricular biopsies were stained with modified Trichrome and Congo-red. Extracellular matrix was quantified with TissueFAXS and HistoeXtreme analysis.

Results: Extracellular matrix by TissueFAXS was 43 ±8.2 ±20.8% of the region of interest, ECV as determined by MOLLI was 33 ±6.9 ±9%. The average post-contrast T1 time by the multiple breath-hold sequence was 407 ±85ms and native T1 times were 900 ±161ms.

The amount of extracellular matrix by TissueFAXS correlated significantly with MOLLI ECV (r=0.583, p=0.001) and with multiple breath-hold post-contrast T1 times (r=0.459, p=0.042), but not with native T1 times (r=0.375, p=0.014).

Conclusion: In the present series, MOLLI ECV appears to be the most accurate method for the quantification of extracellular matrix expansion when validated against myocardial biopsies. Although multiple breath-hold post-contrast T1 mapping may be influenced by renal function, heart rate, and time of acquisition, it also appears useful for non-invasive measurement of extracellular matrix. Native T1 mapping showed the weakest correlation with extracellular matrix by TissueFAXS, but there was a tendency towards a significant relationship (r=0.375, p=0.014).

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In vivo comparison between myocardial fibrosis and myocardial extracellular volume (ECV) measurement by cardiovascular magnetic resonance (CMR)
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Purpose: Myocardial fibrosis is considered as the most important indicator of cardiac damage. Recently, modified Look-Locker inversion recovery (MOLLI) cardiovascular magnetic resonance (CMR) imaging allows for T1 mapping and extracellular volume (ECV) mapping with high level of agreement with histological assessment. The aim of the present study was to compare between % myocardial fibrosis (%F) which was harvested by endomyocardial biopsy from the inferior ventricle and ECV measured using MOLLI.

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**Methods:** A total 16 patients (mean age: 64.0±12.4, male: 15) with non-ischemic heart failure [left ventricular ejection fraction (LVEF) <30%] were enrolled into the present study. %F was defined as fibrosis area/area fibrosis + myocardium area) using Elastica Masson-Goldner (EMG) stain (Fig. 1). A motion corrected myocardial T1 mapping was generated automatically from MOLLI and ECV was estimated from the myocardial T1 values before and after contrast with calibration by blood hematocrit.

**Results:** The patients were divided into two groups according to the median value of %F (median value = 5.69%). Compared to low %F group (n=8), high %F group (n=8) had higher ECV at the inferior segment (median = 30.4 [29th–75th percentile: 20.0–32.5] vs. 36.5 [33.6–41.6], p=0.016) corresponding to the whole left ventricle (30.0 [28.4–31.3] vs. 37.0 [33.4–40.3], p=0.001) (Fig. 1). The patients were divided into two groups according to the median value of %F (median value = 5.69%). Compared to low %F group (n=8), high %F group (n=8) had higher ECV at the inferior segment (median = 30.4 [29th–75th percentile: 20.0–32.5] vs. 36.5 [33.6–41.6], p=0.016) corresponding to the whole left ventricle (30.0 [28.4–31.3] vs. 37.0 [33.4–40.3], p=0.001) (Fig. 1).

**Conclusions:** ECV measured using MOLLI CMR is related to the extent of myocardium fibrosis assessed by LV endomyocardial biopsy in patients with non-ischemic heart failure. ECV measurement can provide non-invasive and quantitative evidence of severity of myocardial fibrosis in these patients.

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**TNative as a marker for differentiation of the left ventricular hypertrophy phenotype of hypertrophic cardiomyopathy and hypertensive cardiomyopathy**


**Purpose:** The differential diagnosis of hypertrophic phenotype remains challenging in clinical practice, in particular between hypertrophy cardiomyopathy (HCM) and increased left ventricular wall thickness (LVWT) due to systemic hypertension (HTN). Its importance lies in the clinical implications for patients. Diffuse myocardial fibrosis is the characteristic feature in HCM, whereas hypertensive response is underpinned by addition of myofibils in otherwise normal myocardial tissue. Late gadolinium enhancement (LGE) imaging provided important new way of differentiation between these two entities by separating those cases with evidence of regional fibrosis. Whereas approximately 60% of patients with HCM reveal visually discernable LGE, T1 mapping is highly discriminative, irrespective of the presence of LGE.

**Methods:** Seventy-nine patients with diagnosis of unequivocally hypertrophic cardiomyopathy and sixty patients with hypertensive cardiomyopathy underwent routine cardiac MRI protocol including assessment of function and scar in addition to T1 mapping (3-Tesla). T1 values were measured conservatively within septal myocardium in midventricular short-axis slice prior to administration of 0.2 mmol/kg of gadobutrol.

**Results:** HCM group showed higher LV mass and maximum LVWT than the HTN group (HCM vs. HTN: LVmass, g/m²: 98.1±33.6 vs. 67.2±22.6; maximum LVWT 19.0±3.9 vs. 13.2±1.3, p<0.0001). LGE was present in 20% (n=10, 4 with an ischaemic pattern) of the HCM group and in 82% (n=48, 2 with an ischaemic pattern) of the HTN group. Patients with HCM showed significantly higher T1 values compared to HTN patients (HCM vs. HTN, msec: 1163±46 vs. 1049±31, <0.001). Native T1 values were concordant to LVWT and LV mass (r=0.52 and r=0.46, p<0.001, respectively). T1 native held superior diagnostic accuracy compared to conventional functional parameters and the presence of LGE to discriminate between hypertrophic or hypertensive cardiomyopathy (AUC, T1 native=0.99, LVMass=0.82, LVWT=0.95, LGE= 0.82, p<0.001). T1 native was identified as an independent discriminator between the two conditions.

**Conclusion:** We demonstrate that T1 native values can reliably discriminate between hypertrophic and hypertensive cardiomyopathy. Given its novelty and ease-of-use nature, T1 native has the immediate potential of clinical translation as a diagnostic marker between these two conditions.

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**Native T1 values in discrimination of subclinical profibrotic phenotype in relatives of patients with hypertrophic cardiomyopathy**


**Introduction and purpose:** Hypertrophic cardiomyopathy (HCM) is associated with significant associated morbidity and mortality. Increased maximal left ventricular wall thickness (LVWT) has been postulated as major risk factor of sudden death; however, relatives with normal LVWT are also at risk. Genetically driven interstitial collagenesis has been proposed as a possible mechanism of diffuse myocardial fibrosis and increased extracellular volume fractions (ECV) has been demonstrated in genotype positive subjects. T1 mapping by cardiovascular magnetic resonance (CMR) provides tissue-dependent relaxation times in line with the underlying myocardial composition. We investigated whether native T1 can also separate genotype positive subjects in the absence of increase in LVWT and how does it relate to ECV measurements.

**Methods:** Seventeen genotype positive first-degree relatives of HCM patients, and seventeen healthy volunteers underwent assessment of T1 mapping, function and scar by CMR at 3-Tesla scanner. T1 values were measured conservatively within the septal myocardium in a midventricular short-axis slice prior to and 15-20 minutes after administration of 0.2 mmol/kg of gadodiamide.

**Results:** Relaties of HCM patients were well matched for age, gender and traditional cardiovascular risk factors. The groups did not differ in the conventional LV parameters, including volumes, left and right ejection fraction or LV mass. None of the studied subjects showed late gadolinium enhancement. Compared to controls, T1 native values were increased in HCM relatives (control vs. relatives, T1 native (msec) 1045±17 vs. 1104±16, p<0.0001), whereas T1 postcontrast and lambda did not vary between groups. Native T1 was identified as the independent discriminator to differentiate between relatives of HCM patients and controls.

**Conclusions:** We demonstrate that T1 native values are increased in genotype positive relatives of HCM patients. We propose that T1 native may serve as an early marker of cardiomyopathy, adding valuable information to genetic testing in this increasing population, possibly without a need for a contrast CMR study.

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**Cardiac amyloidosis: a T1 mapping cardiovascular magnetic resonance study**

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**Background:** Late Gadolinium Enhancement (LGE) technique is currently used for the diagnosis of Cardiac Amyloidosis (CA) by Magnetic Resonance (MRI). Aim of the study was to compare contrast kinetics of interstitial fibrosis on T1 mapping during a short interplay with the underlying myocardial composition. We investigated whether native T1 can demonstrate in genotype positive subjects. T1 mapping by cardiovascular magnetic resonance study.

**Methods:** Thirty-six patients with biopsy-proven systemic amyloidosis (70±9 years, 31 males, 30 immunoglobulin light chain-related, 6 transthyretin-related) and 7 patients with possible amyloidosis (64±10 years, 6 males) underwent evaluation of morphologic and functional features of CA. Conventional LGE images were acquired, with ECV estimation from pre- and post- contrast T1 mapping. Thirty healthy subjects (39±17 years, 21 males) served as controls.

**Results:** Patients with amyloidosis presented increased T1 native of the left ventricle (LVEF) localized, with impaired biventricular systolic function. Among patients with definite amyloidosis, 21 (58%) presented diffuse LV post-contrast enhancement (subendocardial to transmural) and 7 (19%) focal enhancement, while 3 patients (43%) with possible amyloidosis presented focal LV enhancement. Both groups presented a higher cardiac ECV (0.43±0.12 vs. 0.43±0.11 for possible amyloidosis) than controls (0.26±0.04, p<0.05, Fig. 1) and even the patients without LGE presented an ECV significantly higher than controls (0.35±0.10, p<0.01). Myocardial ECV showed an area under the curve of 0.884 in discriminating patients with definite amyloidosis from controls: an ECV of 0.316, corresponding to the 95th percentile of normal subjects, yielded a 79% sensitivity and a 97% specificity.

**Conclusions:** T1 mapping ECV represents a noninvasive direct measure of the amyloid burden with potential utility in early diagnosis and disease monitoring.
980 | BEDSIDE
Characterisation of carotid plaques by in-vivo quantitative T2 mapping: histological validation and lipid quantification
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Background: Multicontrast MRI has emerged as a powerful tool for plaque characterisation. While anti-lipid drugs might reduce plaque lipid measurable by MRI, the non-quantitative nature of multicontrast MRI and its need for extensive post-acquisition processing limits its clinical application. We recently reported the use of quantitative T2 mapping to measure absolute physical properties of different plaque components. Here we sought to validate, at a tissue level, the agreement between T2 mapping and histology; and to evaluate the potential of using T2 mapping for plaque characterisation and its application for lipid quantification. This suggests a potential platform for evaluating the efficacy of lipid active drugs at the level of atherosclerotic plaques.

Methods: 20 patients with >70% carotid stenosis were recruited. Ethics were approved by national and local R&D committee. Black-blood cross sectional 2D images were obtained at 3T. One reviewer classified plaque type using T2 maps with TOF images against the AHA scheme and calculated %lipid area using segmentation algorithm. An independent reviewer processed and evaluated plaque histology and lipid content.

Results: Of 20 patients were excluded due to motion artefacts. Of the remaining 14 plaques, 12 showed exact AHA plaque type matching. The two mismatched cases were due to difficulties in staging intraplaque haemorrhage. An average of 1.9 slices/plaque were used to evaluate lipid quantification. Estimated %Lipid Area from T2 maps was found to correlate with histology with a Pearson correlation coefficient of 0.66 (P<0.001) and the two techniques were found to have good agreement by Bland-Altman analysis with a small bias of 4.02%.

Conclusions: Our study showed the potential of in-vivo T2 mapping for plaque characterisation and its application for lipid quantification. This suggests a potential platform for evaluating the efficacy of lipid active drugs at the level of atherosclerotic plaques.
We tested a multi-biomarker strategy, exploring different underlying physiopathological mechanisms in order to predict thromboembolism in anticoagulated AF patients.

Methods: We studied 949 patients (50% male; median age 76) with permanent AF who were stabilized for at least 6 months on OAC (INRs 2.0–3.0). Levels of high sensitivity troponin T (hsTnT, as index of myocardial damage), N-terminal pro-B-type natriuretic peptide (NT-proBNP, a marker of increased intra-ventricular pressure) and interleukin 6 (IL6, an inflammatory marker) were quantified at baseline, as was von Willebrand factor (vWF, endothelial damage marker) and fibrin monomers (a prothrombotic marker). Patients were followed-up for up to 4 years, and stroke and systemic embolism were recorded.

Results: Median follow-up was 1741 (1281-2285) days; during this period 66 patients had an adverse thromboembolic event (rate 0.03%/year). On multivariable analysis, independent predictors of thromboembolism were hsTnT [HR 1.42 (1.12–1.80), p<0.001], NT-proBNP [HR 1.97 (1.33–2.91), p<0.001] and CHAD2DS2-VASc score [HR 1.19 (1.02–1.40), p=0.03]. The c-statistic for CHAD2DS2-VASc predicting stroke whilst on oral anticoagulation was 0.58 ± 0.04, p=0.023 which significantly increased by adding all biomarkers to 0.66 ± 0.04 (De Long test, p<0.001).

Conclusions: A multi-biomarker strategy is useful in predicting those anticoagulated patients with AF who are at risk of new thromboembolic events, even beyond the CHAD2DS2-VASc score.

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group). 95 (83%) patients had matched intravascular ultrasound examinations allowing change in Maximal Intimal Thickness (MIT), Percent Atheroma Volume (PAV) and Total Atheroma Volume (TAV) to be assessed along with measurement of serum inflammatory markers.

Results: Mean recipient age was 49.9±13.1 yrs. The EVE group (n=47) demonstrated significantly reduced CAV progression as compared to CNI (n=48) [MIT 0.03±0.06 and 0.08±0.12 mm, PA 1.3±2.3 and 4.2±5.05%]. TAV 0.8±14.1 mm² and 12.6±25.2 mm² (all p-values<0.01), respectively. EVE patients had a significantly greater decline in soluble tumor necrosis factor receptor (sTNFR)-1 levels as compared to CNI (p<0.02) but there was no significant difference in change in levels of CRP, VCAM, VEGF, vWf, IL-8 (p>0.05).

Conclusion: Everolimus initiation and CNI withdrawal early after HTx significantly reduces CAV as assessed by IVUS. This strategy appears to have some impact on systemic inflammation as reflected by a significantly greater decline in sTNFR-1. Given the dramatically beneficial effect of everolimus on CAV this novel CNI-free approach should be considered in all de-novo HTx patients.

996 | BEDSIDE
Clinical outcome and predictors of extracorporeal membrane oxygenation (ECMO) support in fulminant myocarditis
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Aims: Limited data are available on the clinical outcomes of patients with fulminant myocarditis complicated by cardiogenic shock that underwent mechanical circulatory support. We evaluated clinical outcome and predictors extracorporeal membrane oxygenation (ECMO) support in patients with biopsy proven fulminant lymphocytic myocarditis.

Methods: From August 2003 to June 2013, total 55 patients with histopathologically proven lymphocytic myocarditis were enrolled in a retrospective, single-center registry. We classified patients into ECMO group (n=27) and non-ECMO group (n=28) according to the use of ECMO for hemodynamic support during index hospitalization.

Results: Overall, patients in ECMO group were higher-risk subjects. 6 patients could not wean off ECMO support. In ECMO group, 21 patients were weaned successfully from ECMO support, 5 patients were expired during ECMO support and 1 patient use bridging ECMO for heart transplantation. In non-ECMO group, 4 patients needed for IABP support, 9 patients needed for inotropics and 15 patients recovered spontaneous. Among in-hospital survivor, there was no congestive heart failure during the follow-up period. But 1 patient in ECMO group expired due to acute myocardial infarction at 25 months. On multivariate analysis, low mean blood pressure at admission (odd ratio [OR] 16.80; 95% confidence interval [CI], 2.09-166.19; p=0.01) and ventricular tachycardia/libration during hospitalization (OR, 43.96; 95% CI, 2.48-778.35; p=0.01) were predictors for requiring ECMO.

Conclusion: In-hospital mortality remains high in patients with fulminant myocarditis needed ECMO support. Low mean blood pressure and ventricular tachycardia/libration might serve as predictors for requiring ECMO.

997 | BEDSIDE
A new wearable textile vest for pulmonary congestion tracking in acutely decompensated heart failure patients: a pilot study
P. Gastelurrutia1, I. Cuba-Gyllesten2, J. Ristami3, E. Zamora4, C. Libre4, A. Caballero4, M. De Antonio5, R. Aarts6, J. Lupon7, A. Bayes-Genis8,1,2,4,9 Germans Trias i Pujol Health Sciences Research Institute, Badalona, Spain;3 Hospital Lariboisiere, Paris, France;4 University Hospital Brno, Department of Internal Medicine and Cardiology, Brno, Czech Republic;5 Helsinki University Central Hospital, Department of Medicine, Division of Emergency Care, Helsinki, Finland;6 National Institute of Cardiology, Intensive Cardiac Therapy Clinic, Warsaw, Poland;7 Attikon University Hospital, Heart Failure Clinic and Secondary Cardiology Department, Athens, Greece;9 INSERM U742, Paris, France;

Purpose: To evaluate a portable wearable biopimpedance vest to track recompensation of acutely decompensated heart failure (ADHF). Pulmonary congestion, a landmark sign of ADHF, may be objectively monitored with transthoracic textile biopimpedance sensors.

Methods: Patients admitted to the cardiology ward with ADHF were screened for inclusion. The four Cole parameters were fitted to the measured bioimpedance using bioimpedance sensors.

Results: Twenty patients were recruited (15% female, mean age 74±9.5 years, left ventricular ejection fraction 37.0±12.5%). Bioimpedance improvement was detected in 90% of patients, and relative changes in bioimpedance during hospital admission properly tracked fluid loss as measured by weight (p<0.001) and clinical severity score (p<0.001). Significant correlations were also found between bioimpedance and other routine parameters of HF severity, such as left ventricular ejection fraction (r=0.450, p=0.047) and NT-proBNP levels (r=–0.41, p=0.038).

Conclusion: Everolimus initiation and CNI withdrawal early after HTx significantly reduces CAV as assessed by IVUS. This strategy appears to have some impact on systemic inflammation as reflected by a significantly greater decline in sTNFR-1. Given the dramatically beneficial effect of everolimus on CAV this novel CNI-free approach should be considered in all de-novo HTx patients.

996 | BEDSIDE
Use of heart failure pharmacotherapy and vasoactive medications in cardiogenic shock in clinical practice - observations from the CardShock study
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Purpose: To analyze real life use of heart failure (HF) pharmacotherapies and vasoactive medications in cardiogenic shock (CS).

Methods: The European multicenter CardShock study prospectively enrolled 220 patients with CS. Data on the use of vasoactive medications within the first 96 hours from inclusion were collected, focusing the analyses to the first 24 hours. In addition, the use of HF pharmacotherapies, such as beta blockers and ACE inhibitors, was analyzed until 24 hours. All-cause mortality was assessed during hospitalization and until 90 days. The data were compared between acute coronary syndrome (ACS) and non-ACS patients as well as to patient characteristics and mortality. Comparisons were performed using χ2 test and Mann-Whitney U test and survival analyses using multivariable logistic regression adjusting for potential confounders.

Results: Mean age of patients was 67 years and 26% were women. Mean blood pressure was 78±47 mmHg and average of mean arterial pressure 57 mmHg. The etiology of CS was ACS in 81% and non-ACS in 19% of patients. HF pharmacotherapies were administered to a notable proportion of patients during the first 24 hours. Intravenous furosemide was given in 65% of patients with a median cumulative dose of 120 mg at 24 hours. Overall, vasopressor or inotrope therapy was administered to 94% of patients. Noradrenaline was the most common vasopressor used (in 75% of patients) followed by dopamine (26%) and adrenaline (21%). The most common inotropes were dobutamine (49%) and levosimendan (24%). Given vasopressors were initiated within the first 24 hours from inclusion in 98% and inotropes in 94% of cases. Vasopressor and inotrope therapies were used simultaneously in 55% of patients and 30% of patients were administered more than one vasopressor. Differences in the use of HF pharmacotherapies or vasoactive medications between ACS and non-ACS patients were scarce. The use of adrenaline within the first 24 hours was independently associated with increased in-hospital (OR 3.6, 95% CI 1.1-11.5) and 90-day mortality (OR 5.1, 95% CI 1.4-18.7). Initial confusion and higher blood lactate level predicted its use (p=0.01) but it was almost invariably used simultaneously with another vasopressor (93/92% (99%)).

Conclusions: As a rule, patients with CS are treated with vasoactive medications and frequently in combination with other vasoactive agents. However, the use of adrenaline is independently associated with increased mortality. This suggests that other treatment strategies should be considered in patients in need of this medication.

997 | BEDSIDE
A new wearable textile vest for pulmonary congestion tracking in acutely decompensated heart failure patients: a pilot study
P. Gastelurrutia1, I. Cuba-Gyllesten2, J. Ristami3, E. Zamora4, C. Libre4, A. Caballero4, M. De Antonio5, R. Aarts6, J. Lupon7, A. Bayes-Genis8,1,2,4,9 Germans Trias i Pujol Health Sciences Research Institute, Badalona, Spain;3 Hospital Lariboisiere, Paris, France;4 University Hospital Brno, Department of Internal Medicine and Cardiology, Brno, Czech Republic;5 Helsinki University Central Hospital, Department of Medicine, Division of Emergency Care, Helsinki, Finland;6 National Institute of Cardiology, Intensive Cardiac Therapy Clinic, Warsaw, Poland;7 Attikon University Hospital, Heart Failure Clinic and Secondary Cardiology Department, Athens, Greece;8 Germans Trias i Pujol Hospital, Badalona, Spain

Purpose: To evaluate a portable wearable biopimpedance vest to track recompensation of acutely decompensated heart failure (ADHF). Pulmonary congestion, a landmark sign of ADHF, may be objectively monitored with transthoracic textile biopimpedance sensors.

Methods: Patients admitted to the cardiology ward with ADHF were screened for inclusion. The four Cole parameters were fitted to the measured bioimpedance using bioimpedance sensors.

Results: Twenty patients were recruited (15% female, mean age 74±9.5 years, left ventricular ejection fraction 37.0±12.5%). Bioimpedance improvement was detected in 90% of patients, and relative changes in bioimpedance during hospital admission properly tracked fluid loss as measured by weight (p<0.001) and clinical severity score (p<0.001). Significant correlations were also found between bioimpedance and other routine parameters of HF severity, such as left ventricular ejection fraction (r=0.450, p=0.047) and NT-proBNP levels (r=–0.41, p=0.038).
Clinical severity was predicted by combining bioimpedance (estimation of a dry lung), heart rate, and Rvco in a naive Bayesian model with AUC = 0.76, as estimated by leave-patient-out cross validation.

**Conclusions:** Serial monitoring of the transthoracic bioimpedance spectrum assessed by texture sensors tracked ADHF reconfiguration during hospital admission. Future studies will confirm whether clinical decision making in ADHF might benefit from this noninvasive, easy-to-use bioimpedance vest.

998 | BEDSIDE
Efficacy of a hospital-primary care integrated heart failure program: a population-based analysis in 56,742 patients
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Introduction and objective: Heart failure programs have proven effective in clinical studies, but its applicability in a real practice environment is more controversial. The present study evaluated the feasibility and efficacy of an integrated primary care-hospital management program in an integrated healthcare area of 309,345 inhabitants.

**Methods:** The analysis included all consecutive patients hospitalized for a primary diagnosis of HF and discharged alive in all hospitals during the period 2008-2010. The 2011 program was implemented and compared mortality and readmissions among patients exposed to the IHFP and all patients exposed to the remaining healthcare areas of the Catalan Healthcare Service.

**Results:** In this study, 56,742 patients were included. There were 181,204 hospitalizations in 2008, where 30% of the patients were exposed to the program, compared to the 54,659 patients exposed to the remaining healthcare areas, had lower risk of death (hazard ratio: 0.92 [0.86-0.97] p < 0.001), lower risk of clinically-related readmissions (hazard ratio: 0.71 [0.62-0.81] p < 0.001) and lower risk of readmissions for HF (hazard ratio: 0.86 [0.80-0.94] p = 0.001). It was observed that the positive impact on morbidity and mortality was more pronounced in the consolidation period of the program.

**Conclusions:** The implementation of multidisciplinary heart failure programs integrating hospital and community is feasible and is associated with a significant reduction in morbidity and mortality of patients.

999 | BEDSIDE
Vasopressin receptor antagonists for the treatment of heart failure: a systematic review and meta-analysis of randomized controlled trials
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Introduction and aims: Heart Failure (HF) and hyponatremia secondary to HF is associated with impaired quality of life, more frequent hospitalizations and with increased all-cause mortality. In the past 10 years, the IV-3 and 2011 trials were performed in this period. In the adjusted analyses, the 2,083 patients exposed to the program, compared to the 54,659 patients exposed to the remaining healthcare areas, had lower risk of death (hazard ratio: 0.92 [0.86-0.97] p < 0.001), lower risk of clinically-related readmissions (hazard ratio: 0.71 [0.62-0.81] p < 0.001) and lower risk of readmissions for HF (hazard ratio: 0.86 [0.80-0.94] p < 0.001). It was observed that the positive impact on morbidity and mortality was more pronounced in the consolidation period of the program.

**Methods:** We identified 13 trials, including 5526 participants. In 10 trials, all patients with cardiac failure received standard therapy for HF, consisting of diuretic treatment, vasodilators and beta-blockers. Two of these trials used furosemide therapy with doses higher than 40 mg daily. In low-quality evidence, vasopressin receptor antagonists in patients with heart failure had no effect on all-cause mortality (RR 0.98; CI 0.88-1.08) cardiac mortality (RR 1.03; CI 0.91-1.16) or change in creatinine (MD -0.01; CI -0.10-0.09 mg/dL), but reduced body weight by 0.8 kg from baseline (MD -0.83; CI -1.10 to -0.55 kg) and increased Na concentration (MD 3.35 mmol/L) in patients treated with placebo. Vasopressin receptor antagonists increased the risk of adverse events by 14% (RR 1.14; CI 1.04-1.26).

**Conclusions:** Vasopressin receptor antagonist may reduce body weight and increase serum sodium concentration but do not improve all-cause mortality, cardiovascular mortality or kidney function. In addition, acceptability of long-term treatment side effects and hospitalization appear problematic.

1026 | BENCH
Forty year changes in cardiovascular risk factors
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**Purpose:** Our country has experienced remarkable changes both in population levels of coronary heart disease (CHD) risk factors and mortality over the past decades. For the national monitoring of risk factors in major non-communicable diseases (NCDs), National FINRISK Studies have been implemented from 1972 to 2012. The purpose is to describe the 40-year changes in cardiovascular disease risk factors.

**Methods:** Study population included participants aged 30 to 59 years in the series on independent random population samples. Data were collected in five-year intervals in 1972-2012. FINRISK studies so far comprised 53,589 men and women who participated in a health examination, gave a venous blood sample, and filled in questionnaires. Serum total cholesterol, systolic and diastolic blood pressure, and body mass index were measured using standardized protocol, and smoking status was recorded.

**Results:** Total serum cholesterol decreased remarkably until the year 2007, but after that has turned to an increased. Systolic blood pressure has continued to decline over time since 1972, while decrease in diastolic blood pressure has levelled off during last ten years. Smoking prevalence has markedly decreased. Body mass index has increased in the population, yet the significant changes occurred in the earlier survey years, not in past 10 years.

**Conclusions:** After three decades of favorable development, the population risk factor levels showed some increase in total cholesterol and diastolic blood pressure. This emphasizes the need for continued efforts towards national disease prevention and health promotion.

1027 | SPOTLIGHT
In Vino Veritas (IVV) Study: Randomized trial comparing long-term effects of red and white wines on markers of atherosclerosis and oxidative stress
M. Taborska1, P. Ostadad2, T. Adam3, D. Rihova2 on behalf of Czech National Telemedicine Center, 1Palacky University, Faculty of Medicine and Dentistry, 1st Dept of Internal Medicine-Cardiology, Olomouc, Czech Republic; 2Na Homolce Hospital, Prague, Czech Republic; 3Palacky University, Faculty of Medicine and Dentistry, Clinical Biochemistry, Olomouc, Czech Republic

Background: Since the early 90s, a growing body of evidence has indicated that the mild to moderate consumption of wine, has a protective effect against cardiovascular diseases.

**Methods:** The IVV study is a first long-term, prospective, multicenter, randomized trial comparing the effects of red (RW) and white wine (WW) on atherosclerosis markers, 146 healthy subjects at mild to moderate risk of atherosclerosis have been randomized to a regular consumption of red wine (Pinot Noir) or white wine (Chardonnay-Pinot) /1 producer, 1 territ for one year (women 0.2 l, men 0.3 l, 5 times a week, logbook for wine and other alcoholic beverages consumption). The primary endpoint is the level of HDL-cholesterol at one year, secondary endpoints are the levels of other markers of atherosclerosis (LDL-cholesterol, C-reactive protein) and oxidative stress (LP-PLA2, Copetoin).

**Results:** The level of HDL significantly decreased at 6 months in WW group in comparison with baseline value (Table 1). We did not detect any differences in the levels of ALT, GGT or bilirubin.

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>Total</th>
<th>White wine</th>
<th>Red wine</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>146</td>
<td>74</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At the enrollment</td>
<td>1.66 (0.58)</td>
<td>1.66 (0.66)</td>
<td>1.65 (0.50)</td>
<td>0.912</td>
</tr>
<tr>
<td>At 6 months</td>
<td>1.58 (0.48)</td>
<td>1.54 (0.52)</td>
<td>1.62 (0.43)</td>
<td>0.317</td>
</tr>
<tr>
<td>Difference</td>
<td>-0.09 (0.34)</td>
<td>-0.14 (0.41)</td>
<td>-0.04 (0.26)</td>
<td>0.074</td>
</tr>
<tr>
<td>p2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 12 months</td>
<td>1.62 (0.49)</td>
<td>1.60 (0.53)</td>
<td>1.64 (0.46)</td>
<td>0.634</td>
</tr>
<tr>
<td>Difference</td>
<td>-0.04 (0.36)</td>
<td>-0.07 (0.42)</td>
<td>-0.01 (0.29)</td>
<td>0.362</td>
</tr>
<tr>
<td>p2</td>
<td>0.188</td>
<td>0.171</td>
<td>0.718</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** In this prospective randomized trial we did not find between long-term mild consumption of red or white wine any clinically relevant differences in the lipid profile, CRP, fasting blood glucose, other markers of atherosclerosis (LP-PLA2 or copen, and liver function tests). Moreover, we were unable to confirm the hypothesis coming mostly from the retrospective studies that wine drinking is associated with elevation of HDL.

The study is registered by ISRCTN under Ref. No. 54359610.
1028  |  BENCH
Coffee or tea consumption: no impact on cardiovascular mortality: the IPC cohort


Purpose: Caffeine, antioxidants and vasodilatory compounds are present in coffee and tea. We aimed to evaluate the impact of chronic coffee or tea consumption on cardiovascular (CV) mortality or non CV mortality, taking into account a large number of potential confounding factors and lifestyle, particularly tobacco consumption, in a large French cohort.

Methods: We included 131,401 subjects (82,117 men and 49,284 women) aged 18 to 95 years who had a health checkup at the Paris IPC Preventive Medicine Center between January 2001 and December 2008. During a mean 3.5±2.2 years follow-up, we observed 95 deaths from CV and 632 from non CV causes. Coffee or tea consumption were assessed with a self-administered questionnaire and classified into three classes: none, 1 to 4, >4 cups per day. Cox multivariate regression model (HR, 95% CI) adjusted for age, gender, educational level, tobacco consumption, physical activity practice, BMI, cholesterol, triglycerides, glycemia, perceived stress and depression scores, systolic blood pressure (SBP), and heart rate were used to evaluate mortality risks.

Results: High-volume coffee consumers (> 4 cups per day) were older than non-consumers (43.7±12.4 vs 39.6±14.6 years) and had more cardiovascular risk factors except for SBP (e.g. 57% vs 17% current smokers). ECG abnormalities were less frequent than in non-consumers. Tea consumption was associated with a better CV risk profile. Lower SBP, cholesterol, BMI, glycemia, Gamma-GT level, and percentage of tobacco consumption and a higher level of physical activity practice were observed among higher tea consumers compared to non-consumers. After adjustment, coffee consumption was not associated with cardiovascular (HR: 1.2 (0.7-2.2) or non CV mortality [0.90 (0.72-1.14)]. For tea consumption, there was no significant association with CV mortality [0.73 (0.44-1.19)]. By contrast, tea consumption was significantly associated with decreased non CV mortality [0.69 (0.58-0.85); p=0.0002].

Conclusion: Although coffee or tea consumptions are associated with better cardiovascular risk factors, particularly blood pressure, than non-consumers, there was no negative association with cardiovascular death. Interestingly, tea consumption was associated with low non CV mortality by comparison with non-consumers who could suggest a less risky lifestyle.

1029  |  BENCH
Chronic periodontal and tooth diseases and cardiovascular mortality in France: the IPC cohort

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Purpose: Periodontal inflammation and tooth loss are linked to cardiovascular prognosis; we aimed to evaluate the relationship between periodontal and tooth status and cardiovascular (CV) and non–cardiovascular mortality (non CV), in a large low to moderate CV risk French cohort.

Methods: The study included 85,110 subjects: 54,346 men and 30,764 women (46.0±13.8 years) who had a standardized health check-up including a dental examination by experienced dental practitioners between January 2002 and December 2008. During a mean 3.4±2.0-year follow-up, we observed 487 deaths, 66 from CV and 421 from non-CV causes. Oral examination included presence of dental plaque, dental calculus, gingival bleeding, number of teeth lost and calculation of an index of masticatory efficiency. Risk of mortality associated with periodontal diseases was evaluated using Cox regression models (HR, 95% CI) including age, gender, educational level, tobacco consumption, glycemia, systolic blood pressure (SBP), gamma-GT, cholesterol, body mass index (BMI), leucocyte count, coffee consumption and physical activity practice.

Results: Periodontal disease or insufficient masticatory efficiency were associated with less favorable cardiovascular risk factors: higher BMI, SBP, glycemia, and tobacco consumption than in controls. Presence of gingival bleeding was associated with an excess risk of CV mortality [2.75 (1.03-7.37)] and non-CV mortality [1.98 (1.29-3.10)]. Dental plaque was associated with an excess risk of non-CV mortality [2.19 (1.27-3.77)] but not CV mortality [0.83 (0.53-1.34)]. Dental calculus was not associated with mortality (non CV and CV). Insufficient masticatory efficiency was not significantly associated with CV mortality [1.78 (0.78-4.06)] but was linked to non CV mortality [1.91 (1.35-2.71)]. There was no effect of tooth loss on mortality.

Conclusion: There was a distinct association between periodontal status/masticatory efficiency and CV risk factors. Independently from cardiovascular risk factors, gingival bleeding as an index of gingivitis was associated with both CV mortality and non-CV mortality. Of note, local inflammation represented by gingivitis was directly associated to CV death, independently from biological markers of systemic inflammation. In contrast, dental plaques and masticatory efficiency were only associated with non-CV mortality and therefore seem to reflect a poorer general health status, rather than represent an additional CV risk marker. Periodontal health status should be regularly assessed, particularly in high CV risk patients.

1030  |  BEDSIDE
Comparing resistant hypertension to smoking in terms of cardiovascular risk: a 3.6 year follow-up study

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Purpose: Resistant hypertension (RHT) has gained great interest in the recent years due to its significant prevalence and need for careful diagnostic and therapeutic approach. The prognostic significance of RHT against other established risk factors such as smoking has not been investigated.

Methods: We followed 2009 treated hypertensive patients without a history of cardiovascular disease for a mean period of 3.6±1.8 years. At the baseline visit, a thorough clinical and laboratory examination was performed. Current smoking was recorded as smoking of at least one cigarette daily, and RHT as office-based uncontrolled hypertension under at least 3 drugs including a diuretic or controlled hypertension under 4 or more drugs. Based on the smoking habits and RHT status, four groups were identified: non-smokers/not having RHT (n=404), 20%, non-smokers/having RHT (n=425), 21% and smokers/having RHT (n=107, 5%). Endpoint of interest was cardiovascular morbidity defined as the composite of coronary heart disease and stroke. The group of non-smokers/not having RHT served as reference.

Results: During follow-up, 69 events occurred (9.6 cases per 1,000 person-years). Incidence rates of cardiovascular events were 5.63 cases per 1,000 person-years in the non-smoker/not having RHT group, 13.45 cases per 1,000 person-years in the smoker/not having RHT group, 13.95 cases per 1,000 person-years in the non-smoker/having RHT group and 15.15 cases per 1,000 person-years in the smoker/having RHT group. Unadjusted analysis showed that non-smokers/having RHT had comparable risk to smokers/not having RHT (HR: 2.2, CI: 1.2-3.9 vs HR: 2.4, CI: 1.3-4.6, p=0.01 for both) while the smoker/having RHT group exhibited the worse prognosis (HR: 2.7, CI: 1.1-6.7, p<0.05). After adjusting for established risk factors, the significant risk of the non-smokers/having RHT group was maintained yet attenuated, while the smoker/not having RHT group exhibited now the worse prognosis.

Conclusions: Smoking and RHT exhibit a similarly significant cardiovascular risk, while, after controlling for established risk factors, the smoker status remains as the most potent predictor among the two. Concurrent risk factors strengthen the cardiovascular risk of RHT to a greater extent compared to that of smoking.
Conclusion: OSA affected the secondary prevention after PCI. However, CPAP treatment can reduce the incidence of MACE.

NEW INSIGHTS INTO THE BASIC MECHANISMS OF CARDIAC ARRHYTHMIAS

**1040 | BENCH**

Spatial-temporal antiarrhythmic effects of verapamil on the development of APD and [Ca2+]i alternans

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Introduction: The appearance of spatially discordant alternans (SDA) can lead to the initiation of ventricular fibrillation (VF). The purpose of this study is to characterize the differences that exist between the development of alternans in the onset of VF before and after verapamil administration.

Methods: Simultaneous optical mapping of voltage and calcium were recorded in four Langendorff-perfused rabbit hearts. APD and [Ca2+]i amplitude (CaA) alternans were initiated using a rapid pacing protocol before and after verapamil administration, starting from a pacing cycle length (PCL) of 350 ms which was reduced until VF induction. APD and CaA alternans were defined as variations of at least 2 ms or 5%, respectively, during at least 10 consecutive beats. The percentage of mapped area that exhibited alternans was measured at each recording and presented as mean and 95% confidence interval (CI). Wilcoxon rank-sum test was used to compare the data between groups.

Results: Verapamil produced a decrease both in the PCL for VF induction (142.5 ± 16 vs. 96.3 ± 18.4 ms) and in the APD of 17.4 ± 4.9 ms during fibrillation. SDA area in the ventricles increased at short PCLs both during baseline and verapamil. However, SDA area was lower during verapamil than during baseline for matched PCLs both for APD alternans (41.6% (95% CI: 26.1 to 57.1) vs 5.4% (95% CI: 0.5 to 11.2), p < 0.005 at PCL=150 ms) and CaA alternans (34.5% (95% CI: 25.4 to 43.6) vs 6.6% (95% CI: -3.1 to 16.3), p < 0.005 at PCL=150 ms), see figure.

Conclusion: Verapamil produces a reduction in appearance of discordant alternans for fast pacing rates and in the pacing cycle length required for VF induction. However, calcium alternans do appear during verapamil infusion at increased higher rates as compared to baseline.

**1041 | BENCH**

Increased trafficking of small-conductance Ca2+-activated K+ channels to plasma membrane modulates action potential duration in human paroxysmal atrial fibrillation

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Background: Small-conductance Ca2+-activated K+ channels (SK channels) have recently been identified in atria, and were implicated in experimental atrial fibrillation (AF). The present study explored the role of SK channels in human paroxysmal AF (pAF).

Methods: Atrial cardiomyocytes freshly isolated from right atrial appendages of neonatal rat ventricular cardiomyocytes (nrCMCs) were isolated from 2-day-old animals and cultured with and without monolayers. To inhibit fibroblast proliferation, cells were treated with mitomycin-C, 1 day after cell isolation. At day 2, cells were transfected with lentiviral vectors encoding either the eGFP alone (LV-eGFP; control vector) or together with a mutant version of Nfat3 (LV-Nfat3-eGFP). Pathological hypertrophy was induced by 24-hour treatments with 100 μM phenylephrine (PE) at day 3 and 8. The pathological nature of the hypertrophy was investigated by analysis of cell surface area (CSA), total protein content and NPPA, Cx43, SERCA2A and Kv4.3 levels. Electrophysiological

primeamine (120 μM) or the anterograde-blocking blocker latrunculin A (1 μM) significantly reduced ISK by 59% and 75%, respectively. Primeamine and latrunculin A had no effect on ISK in inside-out patches excised from HEK293 cells expressing SK channels, excluding direct channel effects of both substances. These data indicate that increased trafficking of SK channels to the plasma membrane contributed to the enhanced ISK in pAF cardiomyocytes. In whole cell-current-clamp recordings with 0.5 μM intracellular Ca2+, action potential duration (APD90) was 30% shorter and apamin-induced prolongation of APD90 was 4-fold larger in pAF than in SR cardiomyocytes, suggesting a contribution of enhanced ISK to APD shortening in pAF.

Conclusions: Our data demonstrated that ISK was enhanced in atrial cardiomyocytes from pAF compared to SR patients and contributed to APD shortening. The ISK upregulation in pAF resulted at least partially from increased trafficking of SK channels to the plasma membrane. Targeting SK channel trafficking may offer a new therapeutic option for AF treatment.

Conclusion: Increased RyR phosphorylation at ser2808 in atrial myocytes from patients with atrial fibrillation may potentiate arrhythmogenic afterdepolarizations in atrial myocytes from patients with atrial fibrillation

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Purpose: Atrial fibrillation (AF) has been associated with increased calcium release from the sarcoplasmic reticulum (SR), but it is not known if there are current changes in the distribution of local release events (calcium sparks) or in the expression of release calcium sensors, RyRs, and the purpose of this study was to investigate whether atrial fibrillation affects the distribution of RyRs, their phosphorylation state, or the distribution of calcium sparks in human atrial myocytes.

Methods: Human atrial myocytes from patients with or without AF were loaded with the calcium indicator fluo-4. Patch-clamp technique was used to clamp the membrane potential at -80mV and measure the membrane current. Calcium sparks were visualized using resonance scanning confocal microscopy at a frame rate of 90 Hz. RyRs were visualized using antibodies against the RyR and RyRs phosphorylated at ser2808 (s2808). RyRs and calcium sparks were detected using custom-made algorithms.

Results: A total of 424 sparks were detected in myocytes from 9 patients with AF 22 and without AF. Sparks were significantly more frequent in myocytes from AF patients (53.2±23 vs. 8.2±2.2 events/min/cell, p<0.01), and this was due to an increased number of spark sites in AF (7.4±3.1 vs. 1.5±0.4 sites, p<0.05). Moreover, the distance from the spark to the cell membrane was significantly reduced in AF (from 2.8±0.4 to 1.6±0.3 μm; p<0.05). Measurement of the SR calcium load by integrating the transient inward current elicited by a rapid caffeine application showed no significant difference between myocytes from 24 patients with AF and 57 patients without AF (7.2±0.7 vs. 8.7±0.4 amol/PF). Furthermore, analysis of the RyR distribution revealed that there was no difference in the density of RyRs from myocytes from patients with and without AF (346 vs. 413 clusters/cell), nor were there any difference in the density of RyRs near the cell membrane (closer than 1.5 μm). However, the density of s2808 clusters increased, resulting in a significantly higher s2808/RyR ratio in myocytes from AF patients (0.56±0.03 vs. 0.33±0.04, p<0.01).

Conclusions: Increased RyR phosphorylation at ser2808 may contribute to increase the calcium spark frequency in myocytes from patients with AF and a resultant shortening of the spark distance to the sarcolemma may contribute to promote spontaneous membrane depolarizations and increase their amplitude.

**1043 | BENCH**

Nfat3 gene transfer to counteract the pro-arrhythmic electrophysiological changes accompanying pathological cardiac hypertrophy

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Background: Small-conductance Ca2+-activated K+ channels (SK channels) have recently been identified in atria, and were implicated in experimental atrial fibrillation (AF). The present study explored the role of SK channels in human paroxysmal AF (pAF).

Methods: Atrial cardiomyocytes freshly isolated from right atrial appendages of neonatal rat ventricular cardiomyocytes (nrCMCs) were isolated from 2-day-old animals and cultured with and without monolayers. To inhibit fibroblast proliferation, cells were treated with mitomycin-C, 1 day after cell isolation. At day 2, cells were transfected with lentiviral vectors encoding either the eGFP alone (LV-eGFP; control vector) or together with a mutant version of Nfat3 (LV-Nfat3-eGFP). Pathological hypertrophy was induced by 24-hour treatments with 100 μM phenylephrine (PE) at day 3 and 8. The pathological nature of the hypertrophy was investigated by analysis of cell surface area (CSA), total protein content and NPPA, Cx43, SERCA2A and Kv4.3 levels. Electrophysiological

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properties, including conduction velocity (CV), action potential duration (APD) and APD dispersion were analysed by optical mapping.

**Results:** PE treatment of rCMC cultures increased mean CSA and total protein content by ∼50%. NPPA levels went up while the amounts of Cx43, SERCA2A and Kv4.3 were reduced. Local 1-Hz stimulation of the rCMC cultures resulted in 38% arrhythmias (i.e. triggered activity) in the PE-treated rCMCs transduced with LV.eGFP (n=56) while PE-treated rCMCs transduced with LV.NFAT3.eGFP showed no arrhythmias (n=59). Following 1-Hz pacing, PE-treated rCMCs transduced with LV.eGFP showed prolongation of repolarization (APD0 and APD80 = 809±46 ms vs. 1573±110 ms and 390 ms in PE-treated rCMCs transduced with LV.NFAT3.eGFP; p < 0.001). Western blot analysis showed that Kv4.3 and Cx43 protein levels were decreased in the hypertrophic rCMC cultures but increased by NFAT3 gene transfer. Mean CSA and total protein content did not differ between the PE-treated rCMCs transduced with control vector or NFAT3 indicating preservation of the hypertrophic phenotype.

**Conclusion:** NFAT3 gene transfer can counteract the PE-induced slowing of CV and Kv4.3 were reduced. Local 1-Hz stimulation of the nrCMC cultures resulted in reduction of pro-arrhythmic features, through APD shortening and lowering of maximum diastolic potential (MDP) upon fusion. CMCs: Our results demonstrate that forced heterocellular fusion of hVSCs with CMCs reduced their pro-arrhythmic features, through APD shortening and MDP lowering by upregulation of voltage-gated potassium channels in hVSC nuclei, mediating stronger outward potassium current. These findings provide new mechanistic insights into anti-arrhythmic reprogramming of scar fibroblasts, which may benefit future anti-arrhythmic strategies.

**1044 | BENCH**

The role of electrophysiological disturbance in the development of stress-induced cardiomyopathy

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**Background:** Stress-induced cardiomyopathy (SIC), also known as takotsubo cardiomyopathy, is characterized by transient regional myocardial akinesis involving up to 2/3 of the heart. This can lead to fulminant heart failure, cardiogenic shock, and literally heart rupture. Although catecholamine-mediated adrenergic overstimulation is indicated in the development of SIC, the pathophysiology leading to cardiac dysfunction of this magnitude is unknown. Excessive catecholamines cause cardiotoxicity to the heart, including electrical disturbance. Patients with SIC indeed have increased risk for electrical abnormalities i.e. QT-segment prolongation, Torsade de Pointe, and ventricular arrhythmias. Therefore, we propose that disability of myocardial contraction in SIC is associated with catecholamine-induced electrical disturbance or electrical silence.

**Method and results:** We have developed SIC-like cardiac dysfunction in rats by a single high-dose injection of isoproterenol (50mg/kg). These rats developed the typical SIC pattern of apical ballooning (apical akinesia) post isoproterenol, imaged with echocardiography. In isolated, Langendorf perfused hearts, monophasic action potentials (MAPs) were simultaneously recorded from the akinetic apex and non-akinet Basin myocardium of the left ventricle. Electrical signals were not silenced but there are changes in the repolarization of the akinetic region that may be related to the increase risk of electrical abnormalities seen in patients. We are investigating the mechanisms associated with these changes.

**Conclusion:**

Lesion formation graph

**Conclusion:** Time was more important issue than contact force in same force-time integral to make adequate ablation lesion formation.

**1045 | BENCH**

Heterocellular fusion of human ventricular scar cells with neonatal rat cardiomyocytes ameliorates pro-arrhythmia through APD shortening and MDP lowering by enhanced outward potassium current

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**Purpose:** Fibroblasts can be pro-arrhythmic due to their detrimental effects on cardiomyocyte electrophysiology through several mechanisms that rely on suboptimal adhesion into the cardiac syncytium. To fully force integration of fibroblasts into the cardiac syncytium, the feasibility of heterocellular fusion between fibroblasts and cardiomyocytes as a novel anti-arrhythmic strategy was investigated.

**Methods:** Human ventricular scar cells (hVSCs) were isolated from patients undergoing redo percutaneous atrial fibrillation ablation: are they important? D. I. Di Biase1, J.D. Burkhardt2, J. Sanchez2, R. Horton3, C. Trivedi2, P. Mohanty2, S. Mohanty2, P. Santangelo2, B. Salwa4, A. Natalie5, 1 Texas Cardiac Arrhythmia Institute at St David Medical Center, Un. of Texas and University of Foggia, Austin, United States of America; 2Texas Cardiac Arrhythmia Institute at St David Medical Center, Austin, United States of America; 3 Texas Cardiac Arrhythmia Institute at St David Medical Center, Austin, United States of America; 4University of Pennsylvania, Philadelphia, United States of America; 5California Pacific Medical Center, San Francisco, United States of America

**Introduction:** Surgical Maze is increasingly being performed for the treatment of atrial fibrillation (AF). We sought to assess the need of ablation of non pv triggers...
to achieve freedom from AF at the long term follow up in patients undergoing repeat catheter ablation following a failed surgical procedure.

Methods: 113 patients undergoing redo ablation for atrial fibrillation after a failed surgical maze ablation were enrolled in this study. Besides to pulmonary vein re-isolation and CFAEs ablation, non PV triggers were elicited with isoproterenol challenge. In 61 pts (group I) non PV triggers were always ablated irrespective of their location, while in 52 pts (group II) non PV triggers were ablated with the exception of the left atrial appendage (LAA). All patients were followed up for at least one year with holter monitoring and event recorders.

Results: After the first ablation procedure, 60 (53.1%) patients were recurrence free at 12 months follow up. When stratified by LAA isolation, success rate was 69% (42/61) in Group I, and 34.6% (18/52) in Group II (p<0.001). Out of the 34 patients with recurrence in Group II, 30 patients underwent repeat catheter ablation. Recurrence from the LAA triggered in 5 of patients who had triggers firing from the LAA, which was isolated. Overall, after LAA isolation, success rate with 1.77 procedures (1.59-1.95) was 86% after a mean of 28.1 months follow up.

Conclusions: Our study demonstrate that in post Maze patients experiencing recurrence of AF, non PV triggers from the left atrial appendage are an important source of AF and their ablation is critical to achieve long term freedom from atrial arrhythmias.

P1048 | BENCH
Global contact mapping plus ablation of the left atrium for the treatment of atrial fibrillation: a novel multielectrode catheter system
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Purpose: A novel single-catheter multielectrode system (Globe) was developed for the mapping and ablation of atrial fibrillation (AF), i.e. multi-electrode high-density contact mapping (e.g. voltage mapping, rotor mapping) plus radiofrequency (RF) ablation (e.g. pulmonary vein isolation (PVI), substrate modification).

Methods: The system consists of an array with 20 ribs containing up to 275 gold electrodes, which can be expanded within the body of the left atrium (LA) to a spherical, partially compliant device that contacts the atrial wall in a stable position. The system allows for continuous real-time electrophysiological and biological mapping of the whole atrium. RF energy can be applied simultaneously at multiple electrodes as required for the individually tailored ablation of target tissue. The tracing of the ablation sites and subsequent ablation can be done remotely in the control room. RF power output is determined by the system based on electrode contact and is regulated by varying energy application duration and temperature. The temperature sensors are located 25 μm behind each electrode. After extensive in-vitro testing, the catheter was deployed in-vivo in 5 canines for mapping and ablation.

Results: In in-vitro studies, the mean lesion depth measured 3.2 ±0.4, 3.7±0.4, 4.1±0.4, 4.8±0.3, and 5.1±0.3 mm, respectively, depending on the temperature set point of 53, 55, 57, 59, and 61 °C. In in-vivo studies, ablation lesion creation parameters ranged in temperature from 52-59 °C with application times of 60-80 seconds. Successful isolation was achieved in all 5 animals, even when adenosine testing was used. Continuous “wave mapping” allowed for on-line observation of LA activation spread during ablation and for on-line confirmation of PVI or isolation of other targets (e.g. “box” isolation). Two animals were sacrificed immediately after the procedure while the other three were survived up to 68 days. Contiguity of lesion lines and lesion transmurality was confirmed by histology. Contiguity of lesion lines: The Globe array is a completely new catheter concept permitting simultaneous high-density multielectrode contact mapping of the entire LA plus RF ablation for both PVI and substrate targets (e.g. rotors) with a single device. The lesions created in the system with the animals caused acute PVI. Chronically, the lesions were shown to be contiguous, transmurral and durable.

P1049 | BEDSIDE
What will be new from antiarrhythmic drug therapy one-year after catheter ablation of atrial fibrillation - J-CARAF
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Purpose: Some patients receiving catheter ablation for atrial fibrillation (AF) suffer from very late recurrence (VLR; initial recurrence >12 months after AF ablation), but its pathophysiology has not been fully elucidated. We analyzed the left atrial functional nonparoxysmal AF patients who underwent catheter ablation by multi-detector computed tomography (MDCT).

Methods: We retrospectively evaluated 63 patients who underwent initial ablation for drug-refractory persistent or longstanding-persistent AF and had no recurrence in the initial year after ablation. We followed them for average 3.2±1.5 years and divided them into 2 groups based on the presence of VLR (VLR-group and NR-group). All patients were submitted to 256-slice MDCT scan before and 3 months after ablation, and estimated LA volume including maximum and minimum volume during cardiac cycle (LAMaxV, LAMinV) and LA emptying fraction.

Results: Out of 63 study subjects (60±10 years, 52 males), 21 patients experienced VLR. There was no significant difference between the groups in LV size, LA volume, or gender proportion. The reduction rate of LAMaxV after ablation was significantly greater in NR-group than in VLR-group (25±1.9% vs. 5.1±18%, P<0.0002). Higher post-LAMinV was associated with higher risk of VLR. (Hazard ratio=1.0169 [95%CI: 1.0074-1.0263], P<0.0005).

Conclusion: Poor reverse remodeling after ablation was a risk factor of VLR. Improvement of left atrial function may be an important marker to evaluate the effectiveness of catheter ablation.

P1050 | BEDSIDE
Can we predict very late recurrence after catheter ablation for nonparoxysmal atrial fibrillation? Analysis of left atrial function with multi-detector computed tomography
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Purpose: We will evaluate what factors are related with AAD-free survival. AAD, statin, renin-angiotensin-aldosterone system blockade, and beta blockade prescribed at the time of discharge failed to show favorable affect on the outcome, while paroxysmal AF (PAF) (68.4% vs. 56.6%, p=0.000), history of prior AAD therapy (76.9% vs. 81.1%, p=0.020), left atrial (LA) diameter (40.1±6.8 mm vs. 41.5 ± 6.7 mm, p<0.001), procedure time (3.37±1.11 vs. 3.72±1.30 h, p=0.000), lack of CFAE ablation (10.1% vs. 16.3%, p=0.002) or LA linear ablation (19.6% vs. 27.1%, p<0.005), and elimination of inducible AF (46.4% vs. 37.4%, p=0.000) were significantly associated with AAD-free survival. In multivariate logistic regression analysis, only PAF (OR 1.35 [1.02-1.79], p<0.05) and procedure time (OR 0.81 [0.73-0.90], p=0.000) were significant predictors of AAD-free survival.

Conclusions: One-year after ablation, two-thirds of patients were free from AAD without re-ablation. No pharmacological treatment at the time of discharge showed any influence on the outcome. PAF and longer procedure time were independent predictors of AAD-free survival.

P1051 | SPOTLIGHT
Botulinum toxin injection in epicardial fat pads can prevent recurrences of atrial fibrillation after cardiac surgery: results of a randomized pilot study
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Background: Animal models suggest that botulinum toxin injection into the epicardial fat pads suppressed atrial fibrillation (AF) inducibility. The aim of this study was to investigate whether intramyocardial injection of botulinum toxin can prevent recurrences of atrial fibrillation after cardiac surgery.
Catheter ablation of atrial fibrillation is associated with decreased LA volumes and improved LV filling pressures and diastolic relaxation pattern.
Results: The alcoholics had larger end-systolic and end-diastolic dimension, thicker interventricular septal and posterior wall and higher LV mass index. However, there were no differences in end-systolic and end-diastolic dimension, and LV mass index among alcoholics. Ejection fraction did not differ between groups. G-LS was lower in alcoholics (p < 0.001) (Figure). We found that G-LS was significantly lower among alcoholics while LV mass index and LV dimensions remained unchanged. While G-ESys was lower in the alcoholics than in the control group (p = 0.03), there were no differences in G-SRearly and G-SRate values. There was a significant correlation between G-LS values and TLDE (r = 0.49, p < 0.001).

Conclusions: This study is the first demonstrating, by 2D-STE, the presence of early functional abnormalities of longitudinal systolic function in chronic alcoholic patients. These functional abnormalities have a parallel development with the increase of alcohol consumption.

P1055 | BEDSIDE
Characterisation of the octogenarians presenting to the incident heart failure clinic
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Purpose: The prevalence of heart failure (HF) rises with advancing age, and peak among the octogenarians. We investigated the characteristics of the patients aged 80-89 years presenting to the incident HF clinic. Methods: We interrogated the incident heart failure clinic data-base serving a city with 550,000 inhabitants. Patients with suspected HF whose natriuretic peptide (NT-proBNP) value >400 pg/ml (ng/l) receive an echocardiogram and a clinical assessment by a heart failure cardiologist. We collected data on the patients seen between 14th of April 2012 and 31st of January 2014. We concentrated on the patients aged 80-89 years, and classified the patients according to the rise of NT-proBNP, NYHA class and cardiac dysfunction.

Results: We saw 1269 patients, of whom 522 patients (41%) were octogenarians. The male/female ratio is 1:1.3. There are 332 patients (64%) with NYHA classes II-IV. The co-morbidities were: Chronic kidney disease (CKD stage III-IV) (42%), systemic hypertension (43%), diabetes mellitus (12%), chronic obstructive pulmonary disease (8%), cerebrovascular accidents (7%) and dementia (3%). The diagnoses were: 110 patients (21%) did not have HF, 191 patients (37%) had HF due to left ventricular systolic dysfunction (LVSD), 156 patients (30%) had HF with preserved left ventricular ejection fraction (HFPEF), 38 patients (7%) had HF due to pulmonary hypertension, and 27 patients (5%) had HF due to valvular disease. The management of the patients was varied (75%) as a result of their attendance at the incident HF clinic, and 13% of them were followed up by the cardiologists. It appears that NYHA class rather than the rise in NT-proBNP or the number of co-morbidities dictated the frequency of changes in the management being offered.

Conclusions: HF-LVSD, and not HFPEF, is the most common HF diagnosis amongst the octogenarians. The NYHA functional class is the main determinant of the frequency of changes made to their management.

P1056 | SPOTLIGHT
Prognostic role of new parameters derived from cardiopulmonary exercise test beyond the oxygen consumption
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Purpose: To assess the prognostic value of two new cardiopulmonary exercise test (CPET)-derived variables in patients with chronic heart failure (CHF): peak circulatory power (PCP) and peak oxygen uptake efficiency (%VO2 max).

Methods: We retrospectively studied 325 consecutive CHF pts, referred to our outpatient clinic: M/F=266/59, aged 52±11 years, ischemic etiology: 115 patients (35%), NYHA III-IV: 74 (24%), mean LVEF: 32.92±10.61%, in sinus rhythm 250 (77%), receiving beta blockers: 298 (91.7%), and ACE inhibitors: 233 (71.6%). All patients underwent clinical examination, blood sampling for assessment of NT-proBNP plasma levels, 2D echocardiogram, six-minutes walking test and peak symptom-limited CPET at cycle ergometer using an incremental symptom-limited protocol. We divided our study population into four groups according to the median value of PCP (group A and B: with PCP >- 1939 mmHg/ml/kg/min, respectively) and the median value of peak VO2 (group C and D: with peak VO2 < 27.7 ml/kg, respectively).

Results: Compared to group B, patients of group A (163/325) had worse functional and clinical status, exercise capacity and ventilator efficiency than (LVEF % 30,68±8.74 vs 35.67±12.30 p<0.0001; NYHA III/IV 75 vs 23 <p<0.0001; NT-ProBNP values 1076±1491.97 vs 478.04±524.54 pg/ml p<0.0001; Watt max (68-153 mg/dL), and 1.79 <8.2-73) for levels <99-153 mg/dl, versus levels >34th percentile -85mg/dl (p<0.001). Lipoprotein(a) levels were elevated among carriers of rs10455872 and rs3798220 minor alleles, and of low number of KIV-2 repeats (trend, all p<0.001). Combining all genotypes, instrumental variable analysis yielded a genetic relative risk for heart failure of 1.18 (95% CI, 1.04-1.34) for a 10-fold lipoprotein(a) increase, comparable to the corresponding observational hazard ratio of 1.22 (1.11-1.35). Upon exclusion of participants diagnosed with myocardial infarction or aortic valve stenosis, risk estimates were attenuated.

Conclusions: Elevated lipoprotein(a) levels associate with increased risk of heart failure with genetic evidence of causality. The association appears mediated, at least partly, via increased risk of myocardial infarction and aortic valve stenosis.

P1057 | BEDSIDE
Elevated lipoprotein(a) levels, LPA risk genotypes, and increased risk of heart failure – a general population study in 98 097 individuals
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Purpose: Elevated lipoprotein(a) levels represent a genetically determined risk factor for myocardial infarction and aortic valve stenosis. We aimed to determine whether elevated lipoprotein(a) levels and corresponding LPA risk genotypes (rs10455872, rs3798220, kringle IV type 2 repeat polymorphism) are associated with increased risk of heart failure, which is presently unknown.

Methods: We combined data from two general population studies (1991-2013; 2011-2013) including a total of 98097 participants, of whom 4122 were diagnosed with heart failure. We conducted observational and genetic instrumental variable analyses in a Mendelian randomization study design to assess evidence of causality.

Results: Elevated lipoprotein(a) levels were associated withmultivariable adjusted hazard ratios of heart failure of 1.10 (95% confidence interval: 0.97-1.25) for 34th to 66th percentile levels (8-19 mg/dL), 1.24 (1.08-1.42) for 67th to 90th percentile levels (20-67 mg/dL), 1.57 (1.32-1.87) for 91st to 99th percentile levels (68-153 mg/dL), and 1.79 (1.62-2.73) for levels >99th percentile (>-153 mg/dl), versus levels <34th percentile (-85mg/dl) (trend, p<0.001). Lipoprotein(a) levels were elevated among carriers of rs10455872 and rs3798220 minor alleles, and of low number of KIV-2 repeats (trend, all p<0.001). Combining all genotypes, instrumental variable analysis yielded a genetic relative risk for heart failure of 1.18 (95% CI, 1.04-1.34) for a 10-fold lipoprotein(a) increase, comparable to the corresponding observational hazard ratio of 1.22 (1.11-1.35). Upon exclusion of participants diagnosed with myocardial infarction or aortic valve stenosis, risk estimates were attenuated.

Conclusions: Elevated lipoprotein(a) levels associate with increased risk of heart failure with genetic evidence of causality. The association appears mediated, at least partly, via increased risk of myocardial infarction and aortic valve stenosis.
Conclusions: Although both PCP and POUE are able to identify, in CHF patients, those with poorer clinical and functional status, only PCP showed a strong predictive value for major adverse events in this subset of patients.

P1059 | BEDSIDE
How objective is NYHA classification? A literature review comparing NYHA class with cardiopulmonary exercise testing
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Purpose: The New York Heart Association (NYHA) classification is commonly used by physicians and studies all over the world. However, it is open to interpretation by both physicians and patients, which can influence its reliability. We aim to review the literature on all studies done with NYHA class and its corresponding cardiopulmonary exercise testing (CPET) results, and thus assess the objectiveness of NYHA in assessing functional class in heart failure patients.

Methods: We ran a PubMed search of “Comparison of NYHA to CPET,” “NYHA and CPET,” and “heart failure and CPET” - yielding 321 papers. 39 studies comparing CPET results in each NYHA class were included. 282 papers were excluded, with 81 studies describing CPET values in combined NYHA classes and 201 studies failing to compare NYHA to CPET. In the majority of studies, only the peak oxygen consumption (VO2) data was complete and was thus the main variable we included for analysis. We then obtained the mean and standard deviation of peak VO2 for each NYHA class for each paper and compared them across. Results: A total of 37 studies were included (6 USA, 22 Europe, 7 Asia, 2 South America), with a total of 3454 patients (1633 males, mean age 57.4 ± 9.0yrs old). The mean peak VO2 was 23.7 ± 4.7 mL/(kg min) in NYHA I patients, 17.4 ± 2.5 mL/(kg min) in NYHA II patients, 12.9 ± 2.3 mL/(kg min) in NYHA III patients and 11.9 ± 2.1 mL/(kg min) in NYHA IV patients. There was substantial overlap between peak VO2 values in each NYHA class (see Fig. 1), especially between Class II, III and IV.

Conclusion: The NYHA classification is intrinsically subjective which is dependent on the patient’s reported symptoms and the evaluator’s interpretation. More objective measurements like CPET may be used additionally to better assess patients.

ADVANCES IN IMAGING OF CONGENITAL HEART DISEASE

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Aortic root asymmetry in Marfan syndrome implies significant disparities between echo and MRI measurements
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Purpose: We aim to evaluate the presence of aortic root asymmetry in Marfan syndrome and its impact on the correlation between echo and MRI measurements.

Methods: MRI and echocardiographic studies were performed in 127 non-operated Marfan patients. Mean time between studies was 9.1 ± 16.2 years. Aortic root diameter was measured by echocardiography using the leading-edge to leading-edge approach at end-diastole. The three cusp-to-commissure aortic root diameters were measured at end-diastole from the axial cine-MRI images and averaged (ARav). Symmetry was defined as a difference ≥3mm among the three aortic root diameters by MRI.

Results: 127 Marfan patients were included (age: 26.2 ± 13.7yrs; 76 females, 59.8%). Mean aortic root by echocardiography (ARecho) was 35.2 ± 6.2mm. The mean averaged aortic root diameter (ARav) by MRI was 34.9 ± 8.8mm and maximum (ARmax) was 35.9 ± 8.1mm. Asymmetry was present in 30 patients (23.6%). In these, the greatest aortic root diameter was LC in 12 (40.0%), NC in 11 (36.7%) and RC in 7 (23.3%). Asymmetry was present in 13 (52.0%) patients with ARecho >42mm (n=25) compared to 17 (16.7%) patients with ARecho <42mm (p=0.001). ARecho was highly correlated with ARav by MRI (r=0.966, p<0.001) and with ARmax (r=0.964, p<0.001).

Mean difference between ARecho and ARmax was 1.4 ± 1.7mm in the asymmetric and 0.6 ± 1.6mm in the non-asymmetric patients (p=0.018). Among patients with an asymmetric aortic root, 5 (16.7%) had a difference ≥3mm between ARmax and ARecho.

Conclusions: Aortic root asymmetry is common in Marfan patients. In the presence of aortic dilatation, aortic asymmetry is more frequent and implies a marked difference between echo and MRI aortic root measurements. Therefore, in the presence of aortic dilatation, MRI should be performed to rule out aortic root asymmetry and determine the best imaging technique for aortic root enlargement follow-up.

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Delayed enhancement cardiac MRI identifies ventricular dysfunction and impaired regional myocardial mechanics in univentricular heart diseases
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Background: The impact of myocardial fibrosis on cardiac performance and clinical outcomes in patients with a functional single ventricle before stage-3 (Fontan) is unknown. Objective- The purpose of this study is to evaluate the relationship between myocardial fibrosis identified by cardiac magnetic resonance imaging (CMR) and ventricular performance in patients before Fontan operation.

Methods: Seven-teen patients with functional single ventricle who are undergoing Fontan operation had CMR study with the myocardial delayed enhancement imaging were prospectively examined from May 2013 to January 2014. Late gadolinium enhancement (LGE) was defined by the lack of ventricular mass. To identify regional wall motion abnormalities, ventricle circumferential strain (CS) was assessed using commercially available zioStat2 (Ziosoft).

Results: Of 17 patients (mean age at study was 3.2 ± 0.8 years), 5 (29%) had positive LGE (LGE+). Of these patients, those with LGE+ had lower ventricular CS compared with those without LGE (LGE-). Patients with LGE+ have shown to have lower ventricular CS compared with the area without LGE (basal: -1.9 ± 1.9% vs. -0.1 ± 3.0%, P=0.046; mid: -3.9 ± 2.1% vs. -8.0 ± 3.9%, P=0.007; apical: -3.9 ± 2.4% vs. -8.2 ± 2.8%, P=0.004). Compared with LGE- group, LGE+ group had decreased ventricular ejection fraction (28.7 ± 9.4% vs. 38.1 ± 9.9%, P=0.04) as well as higher levels of BNP (90.3 pg/ml vs. 30.6 ± 9.4 pg/ml, P<0.001). In addition, patients with LGE+ had higher score of Ross classification (2.4 ± 0.55 vs. 2.0 ± 0.02, P=0.02) and New York University Pediatric Heart Failure Index (14.6 ± 3.8 vs. 7.9 ± 1.3, P<0.01) than in LGE- group.

Age at stage-2 palliation was significantly older in patients with LGE+ group than LGE- subjects (18.5 ± 15 months vs. 8.5 ± 3.4 months, P=0.045). Post-operative course was not significantly changed between LGE+ and LGE- groups (ICU stay: 6.2 ± 2.5 days vs. 8.1 ± 1.8 days, P=0.1; hospital stay: 36.2 ± 1.0 days vs. 37.8 ± 18.4 days, P=0.06).

Conclusion: In this pre-Fontan CMR study, the age to stage-2 palliation may substantially contribute to myocardial fibrosis. The area of LGE was associated with impaired regional CS as well as disturbed ventricular performance. Further studies are needed to examine the possible specificity of LGE as a predictor of heart failure and latent myocardial dysfunction in long-term outcome.
Quantitative assessment of systolic right ventricular function using longitudinal strain in patients with a systemic right ventricle


Purpose: Late systolic dysfunction of the systemic right ventricle (RV) in patients with transposition of the great arteries (TGA) after Mustard operation (TGA-Mustard) and in patients with congenitally corrected TGA (cc-TGA) is of major concern. We evaluated RV peak systolic longitudinal strain (LS) in these patients, compared it to healthy controls and assessed its relation with conventional echocardiography, electrocardiography and NT-proBNP. Methods: Echocardiography, echocardiography and NT-proBNP measurement were performed on the same day in patients with TGA-Mustard or cc-TGA. Echocardiography was also performed in healthy controls. LS was analyzed with use of speckle-tracking echocardiography.

Results: We included 66 subjects: 40 patients with a systemic RV with a mean age of 36.7 ± 7.7 years, and 73% male (31 TGA-Mustard patients (34 ± 4 years after corrective surgery) and 9 cc-TGA patients), and 26 age and gender-matched controls. LS of the RV lateral wall was significantly lower in patients with TGA-Mustard (-15.5 ± 3.5%) or cc-TGA (-16.1 ± 3.6%) than in healthy controls (-26.4 ± 4.5%, p < 0.001), as was the LS per RV segment (Fig. 1). LS of the RV lateral wall was lower in patients in NYHA class II than class I, and correlated with RV apex-base diameter (r = 0.54, p = 0.001), RV fractional area change (r = -0.36, p = 0.001), QRS duration (0.43, p = 0.01) and NT-proBNP (r = 0.53, p < 0.001).

Conclusions: The most sensitive marker of subclinical RV myocardial dysfunction in cToF corrected by TAA.

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Main pulmonary artery area limits exercise capacity in patients long-term after arterial switch operation (ASO) for transposition of the great arteries


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Background: Despite excellent contemporary surgical results, exercise capacity is decreased in patients after ASO. This study compared right ventricular (RV) function, outflow tract area, distensibility and pulmonary blood flow (PBF) distribution of ASO patients to controls and correlated these measurements to exercise capacity.

Methods: Participants underwent cardiac magnetic resonance imaging including angiography and flow measurements and cardio-pulmonary exercise testing. RV function, smallest cross-sectional area of the main (MPA), left (LPA) and right pulmonary artery (RPA), LPA and RPA distensibility (relative area change), PBF distribution and percentage of predicted peak oxygen uptake (VO2peak/kg%) were measured.

Results: Sixty-five patients were included (72% male, mean VO2peak/kg% 86.8 ± 19.6%). The table compares ASO patients to controls and shows correlation coefficients to VO2peak/kg% for ASO patients. MPA area indexed for BSA was smaller in patients aged <18yrs (170.9 ± 76.5 compared to 228.5 ± 49.1 mm2/m2, p < 0.01).

Conclusions: In ASO patients, MPA and RPA areas were smaller compared to controls and VO2peak was reduced compared to reference values, while distensibility and PBF distribution remained within normal range. MPA area was strongly correlated to VO2peak/kg%, suggesting that MPA area - rather than branch stenosis - limits oxygen transport in ASO patients.

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Two-dimensional longitudinal strain is a useful index to identify subclinical right ventricular dysfunction at long-term follow up of corrected Tetralogy of Fallot by trans-atrial approach

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Purpose: Late right ventricular (RV) dysfunction remains the main burden of corrected Tetralogy of Fallot (cToF) even after RV-sparing surgical approach (trans-atrial approach, TAA). This study aimed to assess the presence and extent of subclinical RV dysfunction at long-term follow-up in cToF pts who underwent surgical correction by TAA.

Methods: We performed 2D and 3D echo in 25 asymptomatic cToF pts (17 ± 4 yrs, 15M with >10 years follow-up (mean 16 ± 3 yrs) and compared RV function indexes with those obtained in 18 healthy subjects, matched for age- gender- and body size (C).

Results: cToF pts had RV volume overload (RVEDV 94 ± 23 ml/m2 vs 53 ± 23 ml/m2 in C, p < 0.001) due to significant pulmonary regurgitation (PR index 75 ± 11%). In cToF pts, all RV systolic function indexes were impaired in comparison to C: fractional area change (FAC) (38.6 ± 6 vs 45 ± 8%, p < 0.01), TAPSE (16.3 ± 0.33 vs 23.2 ± 0.41 cm, p < 0.001), TDI S' wave (1.01 ± 0.22 vs 1.37 ± 0.24 cm/s, p < 0.001), 2D global longitudinal strain (RLV1) (21.5 ± 2.5 vs 29.4 ± 2.8%, p < 0.001) and 3DEF (52.5 ± 5 vs 56.4% p < 0.01). At ROC curve analysis, RVL1 had the highest predictive power (AUC=0.98, optimal cut-off= -24%, with 87% sensitivity and 100% specificity to separate cToF pts from C. FAC had the lowest discriminative power (AUC=0.72), while TAPSE, TDI S' wave and 3DEF had intermediate AUC values (0.91, 0.87 and 0.73, respectively). However, if compared with normative values recommended by guidelines, RV systolic function would have been classified as normal in most of cToF pts (Fig. 1): 71% by FAC, 67% by TAPSE, 59% by TDI S' and 96% by 3DEF. Conversely, only 4 pts (16%) had RVL1 < -24%.

Conclusions: In the presence of RV volume overload, RVL1 emerged as the most sensitive marker of subclinical RV myocardial dysfunction in cToF corrected by TAA.
Methods: Three groups of patients were compared: Healthy individuals (H, n=54), patients with tetralogy of Fallot with significant pulmonary regurgitation and without pulmonary or right ventricular outflow tract stenosis (PR, n=50) and patients with RV outflow tract or pulmonary stenosis (PS, n=50). Pulmonary stroke volume was determined by PV-MR in PPA and MPA and compared to aortic stroke volume in the ascending aorta (AO). No patient had significant atrial or ventricular shunting.

Results: Median age was not different between groups: 23 (range 7-69) vs. 21 (range 7-50) vs. 20 (range 8-52) years, p=0.3. Bland-Altman analyses revealed for all groups a higher bias for PV-MR of MPA than PPA in comparison to AO flow measurements (table).

Bias was more important in groups with PR and PS than in H. However F-test analyses did not reveal significant differences of the variances (table).

Conclusions: In all groups, determination of pulmonary stroke volume by PV-MR of peripheral pulmonary arteries showed less bias than of main pulmonary artery, however the variances did not differ significantly. We therefore propose to confirm in selected patients pulmonary blood flow measurements of the main pulmonary artery by flow measurements of the peripheral pulmonary arteries.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Healthy individuals</th>
<th>PR vs. Aorta</th>
<th>PS vs. Aorta</th>
<th>PR vs. PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA vs. Aorta</td>
<td>24.6 ± 10.2</td>
<td>28.3 ± 11.8</td>
<td>27.4 ± 9.9</td>
<td>27.9 ± 12.0</td>
</tr>
<tr>
<td>MPV vs. Aorta</td>
<td>24.6 ± 10.2</td>
<td>28.3 ± 11.8</td>
<td>27.4 ± 9.9</td>
<td>27.9 ± 12.0</td>
</tr>
<tr>
<td>Variance (%)</td>
<td>57.4 ± 30.1</td>
<td>51.3 ± 27.9</td>
<td>51.5 ± 37.8</td>
<td>40.7 ± 23.6</td>
</tr>
</tbody>
</table>

F-test: p value

1.4 1.7 1.9

MPCs, main pulmonary artery; PPA, peripheral pulmonary arteries.

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Three-dimensional speckle tracking echocardiographic evaluation of right atrial function in corrected tetralogy of Fallot

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Introduction: Tetralogy of Fallot (TOF) is one of the most frequently diagnosed congenital cardiac abnormalities. It is known that in TOF patients with right ventricular dilation, abnormal biventricular function and biventricular diastolic dysfunction are common. Three-dimensional speckle tracking echardiography (3DSTE) seems to be a promising non-invasive imaging tool for accurate evaluation of global and regional volumes and function of heart chambers. The present study was designed to assess right atrial (RA) volumes and functional properties in patients with corrected TOF by 3DSTE.

Methods: The study comprised 18 consecutive TOF patients (48.2±11.8 years, 6 males). Their results were compared to 18 age- and gender-matched healthy controls (50.3±15.6 years, 10 males). Complete two-dimensional Doppler echocardiography and 3DSTE have been performed in all cases.

Results: Calculated RA maximum (74.1±51.5 ml vs. 37.8±10.1 ml, p=0.006) and RA minimum (58.2±48.6 ml vs. 23.1±7.9 ml, p=0.005) volumes and RA volume before atrial contraction (67.9±51.3 ml vs. 30.2±18.9 ml, p=0.004) were significantly increased in TOF patients. Total (25.7±12.5%; 39.1±8.8%; p=0.007) and passive (10.0±7.0% vs. 19.8±9.0%; p=0.001) RA emptying fractions proved to be decreased in TOF. Global radial (-9.5±11.9% vs. -18.1±15.1%; p=0.007), longitudinal (-10.1±9.9% vs. 20.2±18.8%; p=0.003) and circumferential (-7.9±5.2% vs. 30.8±11.2%; p=0.007) strains were significantly reduced in TOF patients as compared to matched controls.

Conclusions: Significant alterations in RA volumes and functional properties could be demonstrated in patients with corrected TOF by 3DSTE.

REFINING ANTIITHROMBOTIC THERAPY IN CORONARY ARTERY DISEASE

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Analysis of bleeding and thromboembolic risk with concomitant use of antiplatelet treatment in theAMPLIFY trial

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Purpose: The AMPLIFY trial compared apixaban with conventional anticoagulation consisting of enoxaparin followed by warfarin in patients with acute venous thromboembolism (VTE). In this analysis, we examined the impact of concomitant antiplatelet therapy on the risk of major bleeding, the primary safety endpoint, and recurrent VTE or VTE-related mortality, the primary efficacy endpoint, in patients enrolled in the trial.

Methods: Patients who reported concomitant use of antiplatelet treatment at any time during the clinical trial were identified, and rates for the adjudicated primary safety and efficacy endpoints in these patients were compared with those in patients not taking antiplatelet therapy.

Results: Of the 2676 patients treated with apixaban and 2689 treated with conventional therapy, 402 (15%) and 411 (15%), respectively, reported concomitant antiplatelet drug use; primarily with aspirin. In patients taking concomitant antiplatelet therapy, major bleeding occurred in 5 patients in the apixaban group and in 17 patients in the conventional treatment group (relative risk, 0.30; 95% confidence interval, 0.11 to 0.81). In patients randomized to apixaban, the rate of major bleeding in those taking concomitant antiplatelet drugs was 3.0-fold higher than in those not taking these agents (4.1% and 1.4%, respectively). Rates of VTE or VTE-related death were similar in those taking or not taking concomitant antiplatelet drugs in both the apixaban group (3.6% and 2.0%, respectively) and the warfarin group (3.0% and 2.6%, respectively).

Conclusions: Although concomitant administration of antiplatelet drugs produced a proportionally similar increase in the risk of major bleeding in patients randomized to apixaban or conventional treatment, there were fewer major bleeds with apixaban. Thus, the overall safety benefit of apixaban over conventional treatment was maintained in patients taking concomitant antiplatelet drugs. Concomitant administration of these drugs did not appear to influence the rates of VTE or VTE-related death.

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A meta-analysis of non-compliance or planned discontinuation of aspirin and the risk of mortality and non-fatal myocardial infarction in patients with established or at risk of coronary artery disease

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Purpose: Aspirin for prolonged duration is commonly prescribed to patients with a history of or at increased risk of occlusive vascular events (secondary prevention) due to its proven role in reducing mortality and non-fatal myocardial infarction (MI). Non-adherence due to poor compliance; adverse effects or discontinuation due to small clinical reasons may deteriorate outcomes among such patients.

Methods: PubMed and Embase were searched to identify the studies that report discontinuation or non-adherence of aspirin. Studies reporting the hazardous outcomes (all-cause mortality and non-fatal myocardial infarction) were included in the review. Two reviewers independently performed the literature search and data abstraction using a structured template. Effect size in terms of odds ratios were pooled by random effects method. Quality assessment was done as per Cochrane Collaboration’s tool for ascertainment of bias and a funnel plot was constructed to determine the publication bias.

Conclusion: Of the 856 titles were screened, after which 11 observational studies met the inclusion criteria (103,759 patients). 3 studies evaluated aspirin adherence in acute coronary syndrome (ACS), 3 on the discontinuation in peri-operative period (coronary artery bypass graft (CABG) and valvular replacement), 3 in aspirin adherence to drug eluting stents (DES) and 2 on aspirin non-compliance in coronary artery disease (CAD). Pooled overall estimates suggest that aspirin discontinuation/non-adherence is associated with significantly increased risk of death and MI (Hazard Ratio=1.64, 95% CI=1.19-2.25). The risk was highest with DES (HR=3.33, CI=2.41-4.66) followed by ACS (HR=2.00, CI=1.47-2.65) and CABG (HR=1.73, CI=1.32-2.3). Graphical representation delineating temporal trends showed that the risk is present regardless of the duration of therapy.

Conclusion: Aspirin non-adherence is strongly linked with increased mortality and risk of MI among patients with a history of ACS, CAD, DES implantation and peri-operative patients. Efforts should be undertaken to improve the compliance of aspirin in patients at risk of cardiovascular events and controlled clinical trials should be conducted to identify evidence based strategies of improving outcomes in non-compliant patients. Duration of therapy are limited by variable duration of follow up and significant heterogeneity among the included studies.

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Effects of systolic blood pressure levels on risk for strokes in coronary artery disease patients receiving anti-thrombotic combination therapy: JCAD study

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Purpose: There is increasing concern that aggressive anti-thrombotic therapy would increase the risk of stroke in patients with coronary artery disease (CAD),...
particularly in those having elevated systolic blood pressure (SBP). Thus, we investigated the effects of anti-thrombotic therapy and SBP levels on the incidence of stroke in CAD patients registered in JCAD study.

Methods and results: In 12,936 angiographically documented CAD patients, the incidences of ischemic and hemorrhagic strokes were 4.2 and 1.1 per 1,000 patients-year, respectively. Ischemic stroke was increased with SBP elevation in patients not receiving anti-platelet therapy (APT) or warfarin (Fig. 1). APT, particularly dual APT (DAPT), reduced ischemic stroke in patients with SBP > 140 mmHg, whereas the incidence of ischemic stroke was similar among patients receiving warfarin, irrespective of APT and SBP levels. Hemorrhagic stroke was increased in patients receiving warfarin+DAPT with SBP > 140 mmHg, whereas other treatment regimens had the incidences similar to no anti-thrombotic therapy.

Conclusions: APT, particularly DAPT, was useful for prevention of ischemic stroke in CAD patients, especially hypertensive ones. Warfarin+DAPT increased hemorrhagic, but not ischemic, stroke with elevated SBP in CAD patients. Therefore, strict SBP control is recommended in CAD patients receiving warfarin+DAPT.

P1070 | BEDSIDE
Platelet reactivity and circulating platelet-derived microvesicles in patients with acute coronary syndrome following dual antiplatelet treatment
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Purpose: Dual antiplatelet therapy (DAT) with aspirin and P2Y12 receptor inhibitors is the treatment of choice in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). Platelets and platelet-derived microvesicles (PMVs) play a crucial role in the thrombotic proccess. Measuring platelet function is methodologically demanding and measurement of PMVs could therefore offer an additional method to assess platelet function in previously frozen and stored samples from large biobanks. In the present study we investigated how platelet function measured with multiplate and PMVs measured by flow cytometry were affected by clopidogrel treatment in patients with ACS and PCI.
Methods: 200 patients with ACS who underwent PCI were included in the study and venous blood samples were obtained at discharge. All patients were loaded with 600 mg clopidogrel before PCI. Platelets were activated with ADP (6.4 mM) and analyzed by flow impedance aggregometry (WBA; Multiplate™). Aggregation < 47 U (WBA) defined low responders to DAT.
PMVs were measured by flow cytometry (Beckman Gallios) in samples prepared from stored platelet poor plasma (2000g, 20 min in room temperature). Twenty μl of sample were incubated with lactadherin-FITC and CD42a-PE (platelet antigen GPIX) and C62G2P-APC (P-selectin).
Results: Platelet function measured with WBA revealed that 35 of 180 patients (19%) were low responders and 148 (81%) patients were normal responders with clopidogrel treatment. Levels of PMVs were almost two fold higher in the low responder group compared to patient that responded well to treatment (for both CD42a and CD62P, positive PMVs, p < 0.005 and p < 0.004 respectively).
Conclusions: Patients with high on clopidogrel treatment platelet reactivity have elevated levels of circulating PMVs, indicating ongoing platelet activation despite DAT. PMVs can be used as biomarkers to assess platelet function in plasma samples from large prospective clinical studies.

P1071 | BEDSIDE
Prospective evaluation of ischemic and bleeding events in patients with PCI and oral anticoagulation and a matched control group.
The LASER registry of the WG of Thrombosis of the ESC
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Background: The optimal antithrombotic regimen in patients with an indication for oral anticoagulation undergoing stent implantation still has to be defined. We sought to evaluate current practice in these patients and prospectively collect data in patients with OAC and a matched control group without the indication for OAC.
Methods and results: The LASER included prospectively 482 patients with OAC and stent implantation and a matched group (matched for age, gender and indication for PCI) without OAC. The indication for PCI was STEMI in 9.3%, NSTEMI in 31.1% and unstable angina or stable CAD in 59.6%. The predominant indication for oral anticoagulation was atrial fibrillation (78.8%). Triple therapy with vitamin K antagonists (VKA), aspirin and clopidogrel was used in 95.6%, VKA plus clopidogrel in 3.6% and VKA plus aspirin in 0.8%. Compared to he matched control group without the indication for OAC DES were used less often in the OAC group (64% vs. 31%). In-hospital ischemic and bleeding events were not different between the groups. After 3 months only 42% of patients were still treated with triple therapy while 41% were on OAC alone and 16% on dual antiplatelet therapy. Clinical follow-up at 12 months revealed higher mortality in the OAC group.
Conclusions: Triple-therapy is the most widely used antithrombotic regimen in patients with OAC undergoing PCI. OAC, under the indication for PCI, DES are less frequent used in patients with OAC. In patients with OAC mortality but not bleeding is significantly increased at 1-year follow-up.

P1072 | BEDSIDE
Direct and indirect comparison of ticagrelor and prasugrel pharmacodynamic effects: a systematic review and network meta-analysis
Background: A large number of studies have linked on-treatment platelet reactivity to adverse clinical outcomes, particularly coronary ischemic events and stent thrombosis. Since novel P2Y12 inhibitors (prasugrel and ticagrelor) have been predominantly tested on platelet aggregation data on pharmacodynamic comparisons between these two drugs are scarce. Therefore we directly and indirectly compared ticagrelor with prasugrel in a network meta-analysis.
Methods: PubMed, Cochrane, and EMBASE were searched for studies assessing platelet reactivity in coronary artery disease patients treated with ticagrelor and/or prasugrel standard maintenance doses for more than 6 days. Randomized trials and observational studies using prasugrel and/or ticagrelor and providing biological data using VerifyNow P2Y12 Reaction Units (PRU), Platelet Reactivity Index vasodilator-stimulated phosphoprotein phosphorylation (PRI-VASP) or maximal platelet aggregation (MPA) from light transmission aggregometry (LTA) were considered eligible. Summary effect estimates were generated with random-effects modeling to indirectly compare ticagrelor with prasugrel.
Results: Data were extracted from 28 studies (7 articles regarding direct comparison and 21 articles regarding indirect comparison) which included 4119 patients. Mean age was 62±9 years, 75.47% were male. Compared with clopidogrel, both ticagrelor and prasugrel were associated with a decrease in platelet reactivity using VerifyNow (mean PRU difference ≤-2.17 [-2.84 -1.49] and -1.72 [-2.10 -1.35] respectively), VASP (mean PRU difference ≤-1.83 [-2.13 -1.53] and ≤-1.24 [-1.61 -0.86]) respectively) and LTA (mean MPA difference ≤-1.41 [-1.94, -0.88] and ≤-0.86 [-0.98, -0.73] respectively). Direct comparison showed higher platelet inhibition was obtained with ticagrelor compared with prasugrel according to VerifyNow (mean PRU difference ≤-0.96 [-1.30, -0.62], p<0.00001), VASP (mean PRU difference ≤-0.59 [-0.88, -0.29] p<0.00001) and LTA (mean MPA difference ≤-1.03 [-1.46, -0.61] p<0.00001). Indirect comparison found that ticagrelor pharmacodynamic effect was significantly greater than prasugrel according to VASP (p=0.02). A similar, but non-significant trend was found according to VerifyNow and LTA.
Conclusions: Our current meta-analysis suggests that after indirect and direct comparison between ticagrelor and prasugrel, ticagrelor achieved superior platelet inhibition compared with prasugrel.

P1073 | BEDSIDE
A tailored antiplatelet strategy in STEMI patients based on CYP2C19 genotype is feasible in daily practice - POPular Genetics study
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Rationale: Treatment with dual antiplatelet therapy (aspirin plus clopidogrel, pra-
sugrel or ticagrelor) is essential to prevent atherothrombotic events in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI). Although ticagrelor and prasugrel reduce thrombotic events compared to clopidogrel, they increase bleeding risk and costs. Clopidogrel effectiveness varies between patients, partially according to differences in CYP2C19 drug metabolism, but the subset of CYP2C19 *1/*1 (extensive metabolizer) patients clopidogrel seems equally effective as the newer drugs, with less drugs and possibly less bleeding events. The POPular Genetics study tests the hypothesis that CYP2C19 genotype guided antiplatelet is not inferior to the use of ticagrelor or prasugrel, for the combined endpoint of death, myocardial infarction, stroke, stent thrombosis and TIMI major bleeding. However, it is questioned if routine genotyping shortly after pPCI is feasible in daily practice.

Methods: All patients randomized to the genotyping arm of the ongoing open label, multicenter POPular Genetics study (NCT01761786) were included in this analysis. For every patient a buccal swab or blood sample was obtained during or shortly after pPCI to perform genotyping, using the SPARTAN RX point-of-care device, a validated in-house TaqMan StepOnePlus assay or shipment to a study site with genotyping equipment. P2Y12 inhibitors were prescribed according to local protocol and subsequently adjusted according to the genotyping results: clopidogrel in CYP2C19 *1/*1 patients and ticagrelor or prasugrel in patients carrying 1 or more *2 or *3 (loss-of-function) alleles.

Results: A total of 669 patients were included in 4 study sites until November 2013. Of those patients, 331 were randomized to the genotyping group, with CYP2C19 *1/*1 in 232 (70.1%), *1/*2 in 91 (27.5%), *1/*3 in 1 (0.3%) and *2/*2 in 7 (2.1%) patients, respectively. The time between pPCI and the genotyping result was on average 20.44 hours (range 1:50–168:49 hours), with 77.4% of results available within 24 hours after pPCI and 92.4% within 48 hours. The P2Y12 inhibitor was switched according to genotyping result in 47.4% of patients, 28x to ticagrelor or prasugrel and 129x to clopidogrel.

Conclusion: The POPular Genetics study shows that it is feasible to tailor antiplatelet treatment in STEMI patients within 24–48 hours after pPCI according to CYP2C19 metabolizer status in the vast majority of patients. The efficacy, safety and cost-effectiveness of a tailored antiplatelet strategy are under evaluation.

PCI COMPLICATIONS AND PATIENT SUBSETS

P1074 | BEDSIDE
Long-term clinical outcomes after polytetrafluoroethylene-covered stent implantation for coronary perforation

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Purpose: Polytetrafluoroethylene-covered stents (PCS) have improved the inhospital clinical outcomes of patients with coronary perforation. However, there are few reports regarding their long-term outcomes.

Methods: We analyzed data that was retrospectively collected from 19270 patients who underwent percutaneous coronary intervention in our hospital between January 2004 and December 2013. The study endpoints were major adverse cardiac events (MACEs), defined as cardiac death, myocardial infarction, myocardial infarction during the 3 periods (period 1: 2001-2004, period 2: 2005-2008 and period 3: 2009-2012).

Results: From a total of 13,652 patients, 7974 were in the reference group, 5009 were in the PCS group, and 679 were nonagenarians. STEMI was equally prevalent in all 3 groups (50.4%, 50.1% and 50.8%, respectively). Delay from symptom onset to admission was similar across all age groups. Resuscitation use prior to admission decreased with increasing age (reference group 5.6%, octogenarians 9.0%, nonagenarians 14.0%; p < 0.001). Nonagenarians more frequently presented with worse cardiac function (Killip class 2 was 8.3% in the reference group, 11.8% in octogenarians and 16.6% in nonagenarians; p < 0.001), more comorbidities, in particular more renal diseases (reference group 9.1%, octogenarians 18.7%, nonagenarians 27.8%; p < 0.001) and heart failure (reference group 4.9%, octogenarians 9.0%, nonagenarians 14.0%; p < 0.001). During the 3 periods use of PCI significantly increased in all age groups: in the reference group from 56.9% to 79.0% to 84.0%, in octogenarians from 24.1% to 44.5% to 57.2%, in nonagenarians from 6.2% to 9.1% to 18.1%; p < 0.001. In hospital mortality decreased during the 3 periods: in the reference group from 8.1% to 7.0% to 6.9% (p < 0.03), in octogenarians from 16.3% to 12.9% to 12.6% (p = 0.007) and in nonagenarians from 26.5% to 24.7% to 23.0% (p = 0.74). In all age groups, Killip class ≥2 was the most important independent predictor but in nonagenarians it was the only independent predictor of in-hospital mortality.

Conclusion: In very old ACS patients, PCI use showed a marked increase over the past 12 years and in-hospital mortality slightly decreased at the same time. An impaired cardiac function at admission was associated with a worse outcome in all groups, particularly in nonagenarians.
Results: There were 784 (15.5%) STEMI, 2381 (47.0%) NSTEMACS and 1900 (37.5%) CSA. Overall, mean (SD) age was 70.2 (12.3) years and there were 3,483 (69.5%) males. 323 (41.2%) STEMI and 222 (9.3%) NSTEMACS had cardiac shock. 140 (44.3%) of STEMI, 318 (19.5%) NSTEMACS, 118 (9.1%) CSA had a left ventricular ejection fraction <30%. Crude 30-day and 1-year mortality rates were: STEMI 28.9% & 37.6%, NSTEMACS 8.9% & 19.5%, CSA 14% & 7.0%. Unadjusted-in hospital major adverse cardiovascular & cerebrovascular event rates were: STEMI 26.6%, NSTEMACS 6.6%, CSA 3.3%. Risk of 30-day mortality was greater for STEMI and NSTEMACS than CSA (adjusted odds ratio (aOR), 95% confidence interval (CI) STEMI 29.45, 19.37 to 44.80, NSTEMACS 6.45, 4.27 to 9.76). Over 40% of patients presenting with STEMI had cardiac shock, in whom mortality was higher than in STEMI without shock (30-days: 52.0% vs. 11.7%, 1-year: 61.1% vs. 20.9%). Radial, compared with the femoral approach, was associated with 40% lower 30-day mortality (STEMI: aOR, 95% CI: 0.37, 0.21 to 0.62; NSTEMACS: 0.66, 0.45 to 0.97).

Conclusions: Over half of the UPLMS PCI was non-elective and these patients had worse outcomes than elective cases. Cardiogenic shock was present in 40% of STEMI, of whom 52% died at 30-days. The radial approach was associated with lower early mortality in acute cases compared with femoral.

P1077 | BEDSIDE
Do statins prevent contrast induced nephropathy in patients undergoing coronary angiography or percutaneous intervention? A meta-analysis of 7 randomized trials
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Purpose: Contrast Induced Nephropathy (CIN) is a complication of procedures that involve the injection of contrast media, mediated by intravascular endothelial cell lin- cular toxicity from the contrast agent and tubular apoptosis. Statins have been shown to possess pleiotropic effects (anti-oxidant, anti-inflammatory and anti-thrombotic properties). Aim of this meta-analysis is to evaluate the efficacy of short-term statins for the prevention of CIN in patients undergoing coronary an- giography/PCI.

Methods: We performed formal searches of PubMed, EMBASE, Cochrane central register of controlled trials and major international scientific session abstracts from 1990 to 2013 of trials which compares short-term statins versus Placebo for the prevention of CIN in patients undergoing coronary angiography/PCI. Data regarding study design, statin dose, inclusion and exclusion criteria, number of patients, and clinical outcome was extracted by 2 investigators. Disagreements were resolved by consensus.

Results: A total of 7 trials were included. CIN occurred in 5.2% (45/860) of patients treated with statin therapy (OR[95%CI]=0.45 [0.30-0.65], p<0.0001; phet=0.33). The benefits were mostly ob- served with high-dose short-term statin therapy (OR[95%CI]=0.44 [0.30-0.65], p<0.0001; phet=0.16), but not with low-dose statin therapy, (OR[95%CI]=0.63 [0.16-2.44], p=0.50; phet=0.65). By meta-regression analysis, no significant relation- ship was observed between benefits from statin therapy and patient’s risk profile, LDL cholesterol, contrast volume or diabetes rate.

Conclusions: Among patients undergoing coronary angiography/PCI the use of short-term statins reduces the incidence of CIN, and therefore are highly recom- mended even in patients with LDL cholesterol below the recommended threshold.

P1078 | BEDSIDE
Differences in coronary artery disease (CAD) among patients infected with human immunodeficiency virus (HIV) undergoing percutaneous coronary intervention (PCI): results from a single-center registry

Purpose: Premature CAD is a known complication in HIV patients. However, the angiographic features or CAD burden in HIV patients has not been well described. Methods: We compared HIV positive (n=97) patients who underwent PCI over a 9-year period to HIV negative (n=92) patients matched for age, gender, dia- betes and year of PCI. Quantitative coronary angiography (QCA) analysis was performed blinded to HIV status. We also determined the 1-year rate of major adverse cardiac events (MACE) including death, myocardial infarction (MI), and urgent revascularization.

Results: The mean age was 57 years. HIV patients had lower body mass in- dex, worse lipid profile, and presented more frequently with MI (28% vs. 11%, p=0.003). While CAD burden was similar in the two groups (Syntax score, 13.8 vs. 11.7, 6.7, p=0.15), HIV patients had more proximal disease with worse calci- fication (Table). Post-PCI, the residual diameter stenosis was worse among HIV patients (19±8.3 vs. 16±8.3, p=0.02), 1-year MACE was high in both groups (16.5% vs. 13%, p=0.50).

Angiographic characteristics according to HIV status (lesion-level analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV (n=149)</th>
<th>Non HIV (n=139)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>16.9±10.9</td>
<td>15.1±8.8</td>
<td>0.12</td>
</tr>
<tr>
<td>Reference vessel diameter (mm)</td>
<td>2.65±0.70</td>
<td>2.34±0.63</td>
<td>0.0001</td>
</tr>
<tr>
<td>Minimal lumen diameter (mm)</td>
<td>1.86±0.53</td>
<td>1.68±0.44</td>
<td>0.0003</td>
</tr>
<tr>
<td>Diameter Stenosis (%)</td>
<td>67±15.3</td>
<td>71±2.16±5.3</td>
<td>0.02</td>
</tr>
<tr>
<td>Lesion location:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD (vs LCX, RCA)</td>
<td>59 (40%)</td>
<td>58 (43%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Proximal (vs mid, distal)</td>
<td>57 (40%)</td>
<td>36 (27%, p=0.01)</td>
<td></td>
</tr>
<tr>
<td>Heavily calcified (vs no/mild, moderate)</td>
<td>25 (18.1%)</td>
<td>11 (8.1%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Tiffi flow grade 3 (vs 0, 1, 2)</td>
<td>108 (76.6%)</td>
<td>88 (63.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>High risk lesion (vs x)</td>
<td>32 (21.7%)</td>
<td>16 (11.7%)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*p values for >2 group comparisons (comparison groups listed). Abbreviations, LAD: Left anterior descending artery; LCX: Left circumflex artery; RCA: Right coronary artery.

Conclusion: In this first HIV QCA study, HIV patients were more likely to present with acute MI, and displayed multiple angiographic differences in lesion characteristics compared to matched controls. These findings suggest that atherosclerosis and its progression are altered in the setting of HIV.

P1079 | BEDSIDE
Glycemic control for kidney injury prevention after PCI: preliminary results from Eluglycemia for Renal Impairment Prevention after contrast-Medium Exposure (EURIPLE) randomized study

Purpose: Contrast Induced-Acute Kidney Injury (CI-AKI) is one of the most re- curring adverse events after percutaneous coronary intervention (PCI), leading to high morbidity and mortality incidence. Patients affected by diabetes mellitus and/or chronic renal impairment are at higher risk of this complication. Up-to-date, the gold standard for CI-AKI prevention is hydration with isotonic saline solution (ISS) before and after exposure of contrast medium. The role of several protec- tive agents, such as N-Acetyl-Cysteine (NAC) has been largely discussed, with conflicting results. Moreover, poor glycemic control before PCI has been associ- ated with increased incidence of CI-AKI. We sought to evaluate the efficacy of glucose-insulin-potassium (GIK) and NAC, in addition to ISS, for the prevention of CI-AKI in patients undergoing PCI.

Methods: 102 diabetic and/or with chronic renal failure patients has been ran- domized to 3 different protocols: ISS-GIK-NAC (group 1), ISS-GIK (group 2), ISS (group 3). ISS infusion started 12 hours before PCI and maintained up to 24 hours after the procedure. GIK infusion was administered from 12 hours before to 12 hours after the procedure. NAC was given as oral doses of 1200 mg 12 hours and 1 hour before PCI. Blood samples were collected before and after 24 hours after PCI to evaluate serum creatinine (sCr). CI-AKI was defined, according to the RIFLE criteria, as an increase of sCr ≥25% from baseline within 48 hours after contrast administration.

Results: We observed a significant reduction of mean sCr after PCI in the overall population (1.02 mg/dl versus 0.99 mg/dl, p=0.03). In detail, this reduction was observed in group 1 and 2, whereas a slight increase was found in group 3 (-4% in group 1 and 2 and +3% in group 3) (group 1 vs group 3, p=0.01; group 2 vs group 3, p=0.01; p for trend = 0.01). The overall incidence of CI-AKI was 4%, with all the 4 cases in the group 3. The percentage of patients who developed any post-PCI sCr increase from baseline was higher in group 3 compared to other groups (29.4% vs 42% in group 2 vs 54% in group 1; p=0.04).

Conclusions: The results of this study showed an absolute and percentage signifi- cant reduction of sCr after PCI in patients with GIK infusion and NAC admin- istration, in addition to ISS. Our hypothesis is that maintaining a peri-procedural euglycemic state, jointly with the protective action of insulin on kidney metabolism, may play a favorable role in preventing contrast-induced renal impairment in dia- betic and with chronic renal failure patients undergoing PCI.

P1080 | BEDSIDE
Prevention of contrast-induced nephropathy with single bolus erythropoetin in diabetic patients with chronic kidney disease undergoing coronary interventions - a randomized controlled trial
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Purpose: Contrast-induced nephropathy (CIN) is associated with poor outcomes, thus prevention of CIN may be of clinical value. Erythropoetin has been shown...
to be tissue-protective in experimental models and in few clinical studies of acute kidney injury. We therefore evaluated the effectiveness of a single bolus of erythropoietin for prevention of CIN after coronary angiography (CA) and/or percutaneous coronary intervention (PCI) in consecutive diabetic patients with chronic kidney disease who are at high-risk of developing CIN.

Methods: A prospective, randomized, controlled trial was carried out in 120 diabetic patients with eGFR < 60 ml/min/1.73 m² who underwent non-urgent CA with or without PCI. Patients received a subcutaneous single dose of 50,000IU of erythropoietin or standard preventive protocol (normal saline + N-Acetyl-Cysteine) before CA. CIN was defined as an increase in serum creatinine level, compared to baseline value, of at least 0.5 mg/dL during the first 2 days after exposure to contrast media. Primary outcome was the incidence of CIN. Secondary outcomes were the sensitivity and positive predictive value (PPV) of cystatin C (CC) and Neutrophil gelatinase-associated lipocalin (NGAL) for diagnosis of CIN.

Results: The observed incidence of CIN in our study (6%) was significantly lower than the expected for such high risk population. The administration of EPO prior to CA resulted in a trend (yet non-statistically significant) for reduction in CIN (8.3% vs. 4%, p=0.31). The results were independent of baseline kidney function, contrast media type or volume, gender and type of procedure. Cystatin C and NGAL demonstrated a low sensitivity (16.6%) and low PPV (6.7% and 33.3% respectively) for detecting CIN.

Conclusion: The administration of a single dose of erythropoietin prior to CA or PCI resulted in a trend toward reduction in the incidence of CIN; however, the low incidence of CIN among non-urgent patients in our study probably masked the potential renoprotective effect of erythropoietin.

ADDRESSING THE CHALLENGES IN CARDIAC REHABILITATION

P1081 | BEDSIDE Impact of a hospital-based multidimensional educational program early after acute coronary syndromes: A multicentric Swiss prospective trial

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Introduction: Medical societies recommend the development of national programmes to improve secondary prevention in patients with acute coronary syndromes (ACS). We tested the impact of a hospital-based intensive multidimensional educational program (ELIPS) used as add-on to the recommended process care (standard care) for patients hospitalized with ACS.

Methods: The ELIPS intervention comprised a number of actions added to standard care and coordinated by designated leaders at each hospital: (1) a hospital-based multidimensional educational program after acute coronary Syndrome) programme was implemented in 4 main academic hospitals in Switzerland. The ELIPS intervention comprises a number of actions added to standard care and coordinated by designated leaders at each hospital: (1) a patient-centered educational program making use of interactive tools (film, discharge card, informational cards, website, wall chart for motivational interviewing [MI] sessions); (2) training courses for care-providers on MI and cardiovascular health education. In a before-after prospective design, we compared the standard care group (2009–2010) to the ELIPS group (2011–2012) for 1-year adherence to evidence-based therapies (aspirin, beta-blockers, statins, angiotensin-converting enzyme ACE) inhibitors or angiotensin-receptor blockers ARB), attendance to cardiac rehabilitation (CR) and achievement of recommended targets of cardiovascular risk factors (CVRF), adjusting for differences in baseline characteristics.

Results: The observed incidence of CIN in our study (6%) was significantly lower as compared with the controls (n=101; 55.7±10.8 years). Patients in the CR group performed a 8-week training program, under clinic supervision, with 60 minutes sessions (including 30-minutes with an intensity of 70-85% of maximum heart rate), held three times per week. At the start and at the end of the program, all patients were submitted to detailed transthoracic echocardiography (including mitral flow analysis, pulmonic vein flow analysis, tissue-Doppler velocities and 2D and 3D ejection fraction) and cardiopulmonary exercise test (determination of peak VO2, VO2 at anaerobic threshold (AT) and duration of the exercise (p<0.05).

Conclusion: There was no significant impact in functional capacity in the CR group, as determined by peak VO2 and VO2 at AT (1.46±0.39ml/kg/min increase). In the control group, there was no significant change in peak VO2, VO2 at AT or duration of the exercise (p>0.05).

P1083 | BEDSIDE Exercise based cardiac rehabilitation in heart failure patients: an updated meta-analysis demonstrating benefits in hospital admission and exercise capacity

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Background: Guidelines recommend exercise-based cardiac rehabilitation (EBCR) for patients with heart failure (HF). However, research to date has not investigated the longer-term outcomes including mortality and hospitalisation in light of the contemporary management of HF.

Methods: Systematic review including a meta-analysis of EBCR on all-cause mortality, hospital admission, and standardized exercise capacity using four separate exercise tests in patients with heart failure (HF) over a minimum follow-up of 6-months from January 1999 until January 2013. Electronic searches were performed in the databases: Medline, CENTRAL, EMBASE, CINAHL, and PsycINFO constrained to randomized controlled trials (RCTs).

Results: A total of 46 separate RCTs qualified for the meta-analysis, which employed the methods of Mantel and Haenzel or DerSimonian (binary data) or Cochrane (continuous data) methods. The results were independent of basal kidney function, con-
Addressing the challenges in cardiac rehabilitation

**P1084 | BEDSIDE**

**Compliance with cardiac rehabilitation guideline in the netherlands**

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**Purpose:** In 2010 the Health inspectorate conducted a survey on all institutions that offer cardiac rehabilitation (CR) programs in the Netherlands. The number of patients enrolled in a program was too low. Also patients were insufficiently supported in lifestyle changes. The investigation was repeated in 2012. The aim of this investigation was to determine if all institutions that offer a CR program comply with the guideline.

**Methods:** Follow-up was performed between December 2012 and June 2013. All 90 hospitals and 9 rehabilitation centres submitted questionnaires about their program; 14 hospitals without cardiac rehabilitation were questioned about their referral rates. All institutions assessed their CR program using a previous constructed framework of 19 indicators based on the Dutch guideline Cardiac Rehabilitation (2004, updated in 2010). The criteria used were based on the guideline and defined in cooperation with the Netherlands Society of Cardiology.

**Results:** The response rate was 100%. The 76 hospitals increased their intake of patients with a myocardial infarction from 57% in 2009 to 64% in 2012. The referral rates of the 14 hospitals without a CR program rose from 66% in 2010 to 70% in 2012. Registration of individual lifestyle information and data collection at aggregated level improved evidently compared to 2010. However, patient participation in smoking cessation and weight loss programs had not sufficiently increased. Less then half of the institutions had an adequate score. Also the number of patients offered to partake in the lifestyle information program was low, not all institutions offered this program.

**Conclusions:** Non-adherence to cardiovascular morbidity and mortality after ACS. Strategies to promote patient’s referral and adherence to CR programs should be implemented to minimize burden of coronary heart disease.

**P1086 | BEDSIDE**

**Learning and coping strategies improves attendance in cardiac rehabilitation**

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**Background:** Cardiac rehabilitation (CR) in ischemic heart disease (IHD) and heart failure (HF) has a potential to reduce mortality and morbidity and improve quality of life. However, far from all patients complete CR or succeed with lasting lifestyle improvements. Patient education programs which can enhance attendance in CR are needed. A new patient education; learning and coping strategies (LC), was developed.

**Objective:** Aim of this study was to measure the effect of LC strategies on attendance in CR.

**Methods:** The study was designed as an open 1:1 randomised controlled trial with LC strategies applied to standard CR as one of the arms versus standard CR as the control arm. Key points in the LC strategies were: Situated and reflexive education, individual clarifying interviews before and after the program and participation of expert patients in the sessions. The CR program in both arms consisted of eight weeks with training three times a week and education once a week. All sessions lasted one and a half hour. Both arms were initiated and finished with an exercise test on a bicycle and follow up exercise test was performed three month after.

**Results:** In total 827 patients over 18 years admitted with IHD or HF were included. Two patients were excluded. Out of the 825 patients 413 was randomised to the LC group (mean age 63 years, 76% male, 78% with IHD, 22% with HF) to the control group (mean age 63 years, 76% male, 78% with IHD, 22% with HF). There was no difference in age and gender distribution between the groups. In total 412 to the control group (mean age 63 years, 76% male, 78% with IHD, 22% with HF). A significant baseline differences between the groups were found. In total 716 (99%) patients attended the initial exercise test. Out of these 616 patients (85.5%) attended the CR program, defined as completion of the second exercise test at the end of the program. In the LC group 340 (83.3%) attended the CR program compared to 312 (76.5%) in the control group (p=0.018). At three month follow up 313 (76.7%) patients in the LC group completed the exercise test compared to 287 (70.3%) in the control group (p=0.039). Thus attendance was significantly higher (9%) for patients in the LC group. In total all patients attended on average in 19.1 of the 24 planned training sessions. In the LC group 80% attended at least 18 sessions which was significantly higher than the patients in the control group where 73% attended 18 sessions or more (p=0.023). On average all patients attended 6.3 out of the 8 planned education sessions. In the LC group the patients attended on average 6.6 education sessions which was significantly more than 6.0 in the control group (p=0.04).

**Conclusion:** LC strategies applied in CR improves attendance.

**P1087 | BEDSIDE**

**Non adherence to cardiovascular preventive guidelines is associated with all-cause and cardiovascular mortality**

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**Background:** Cardiovascular (CV) disease remains the first cause of prema-
ture death in European countries. Control of CV risk factors is thus mandatory. The purpose of this study was to know the real impact of the non-observance of lifestyle and dietary rules on mortality in primary prevention.

**Methods:** Our study population consisted in patients, both women and men, who had consulted from 1995 to 2011 to the Department of Preventive Cardiology (DPC) of a Southwestern University Hospital. We excluded patients whose age was less than 30 year-old and all patients with established history of ischemic heart disease (International Classification of Disease, 9th revision, codes 410.0-414.9). Questionnaires collecting data on socio-economic level, knowledge of lifestyle and dietary rules, previous medical history, drugs intake, obesity and cardiovascular risk factors were recorded by a trained medical staff. Vital status (causes and date of death) was obtained for each participant through the national database. Multivariable predictive relationships with total mortality were evaluated with the use of a Cox proportional hazards model.

**Results:** 4885 patients were included. 56% were men and the mean age was 53. After a mean follow up of 8.6 years, 129 deaths including 31 CV deaths were recorded. After adjustment for age and gender, ignorance of lifestyle and dietary preventive CV rules was significantly associated with all-cause mortality (Hazard Ratio (HR)=2.16, p<0.001, 95% CI [1.51-3.09]) and with CV mortality (HR=2.28, p=0.020, 95% CI [1.14-4.61]). After adjustment for age and gender, non compliance to anti-hypertensive diet (HR=1.62, p=0.01, 95% CI [1.22-2.33]), anti-diabetic diet (HR=1.78, p=0.034, 95% CI [1.04-3.04] were significantly associated with all-cause mortality. Non compliance to lipid lowering diet was not significantly associated with all-cause mortality (HR=1.40, p=0.25, 95% CI [0.79-2.48]). In multivariate analysis, after adjusting for age, gender, smoking status, diabetes, hypertension and socio-economic status, ignorance of lifestyle and dietary preventive CV rules remained significantly associated with all-cause mortality (HR=1.66, p=0.015, 95% CI [1.10-2.20]). Non compliance to anti-diabetic diet did not remain associated with all-cause mortality (HR=1.75, p=0.065, 95% CI [0.97-3.17]) in the full adjusted model.

**Conclusions:** Ignorance of lifestyle and dietary preventive CV rules was associated with all-cause mortality in primary prevention stressing the potential impact of lifestyle on long-term mortality.

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**CARDIAC AND ARTERIAL REMODELLING IN HYPERTENSION**

P1008 | BEDSIDE

**Free androgen index as a predictor of central hemodynamics and arterial stiffness in postmenopausal women**

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**Background:** Aging increases autonomic imbalance, obesity, and insulin resistance, which contribute to arterial stiffness and central hemodynamics. The aim of the study was to test the hypothesis that free androgen index (FAI) can predict central hemodynamics and arterial stiffness.

**Methods:** We evaluated 150 postmenopausal women (over 45 years old). Participants underwent a comprehensive echocardiography assessment, biochemical parameters, and 48-hour ambulatory blood pressure monitoring. Participants were divided into tertiles of FAI, and were compared regarding central hemodynamics and arterial stiffness parameters.

**Results:** FAI was significantly higher in tertiles with higher FAI (p<0.05). FAI was independently associated with central hemodynamics and arterial stiffness parameters (p<0.001, 95% CI [1.51-3.09]) and with CV mortality (HR=2.28, p=0.020, 95% CI [1.14-4.61]). After adjustment for age and gender, non compliance to anti-hypertensive diet (HR=1.62, p=0.01, 95% CI [1.22-2.33]), anti-diabetic diet (HR=1.78, p=0.034, 95% CI [1.04-3.04] were significantly associated with all-cause mortality. Non compliance to lipid lowering diet was not significantly associated with all-cause mortality (HR=1.40, p=0.25, 95% CI [0.79-2.48]). In multivariate analysis, after adjusting for age, gender, smoking status, diabetes, hypertension and socio-economic status, ignorance of lifestyle and dietary preventive CV rules remained significantly associated with all-cause mortality (HR=1.66, p=0.015, 95% CI [1.10-2.20]). Non compliance to anti-diabetic diet did not remain associated with all-cause mortality (HR=1.75, p=0.065, 95% CI [0.97-3.17]) in the full adjusted model.

**Conclusions:** Ignorance of lifestyle and dietary preventive CV rules was associated with all-cause mortality in primary prevention stressing the potential impact of lifestyle on long-term mortality.

P1010 | BEDSIDE

**The association of left ventricular hypertrophy with intraventricular diastolic dyssynchrony at diastolic phase during exercise in hypertensive patients**

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**Background:** Recent investigations have revealed that even mild left ventricular hypertrophy (L VH) is associated with diastolic dysfunction. The aim of this study was to examine the association of diastolic dyssynchrony with L VH during exercise.

**Methods:** Consecutive hypertensive patients with L VH (n=60) and 30 control individuals were enrolled. Exercise stress echocardiography was performed using a symptom limited, multistage supine bicycle test. Diastolic dyssynchrony was defined as other than 90° and 180° phase differences between at least two LV segments. The time of peak early diastolic velocity at 12 segments (TPe-SD, ms) was measured.

**Results:** TPe-SD was significantly higher in patients with L VH at rest (27.3±11.0 vs. 18.7±7.4 ms, p<0.005) and at peak exercise (42.0±10.6 vs. 30.6±12.4 ms, p<0.001). After applying modified SD, the difference was much more increased (80.0±17.6 vs. 49.0±21.3 ms, p<0.001). Multiple regression analysis showed significant LV mass index (β=0.515, P<0.001) and E/E′ at peak exercise (β=-0.253, P=0.025) were independently associated with LV diastolic dyssynchrony during exercise.

**Conclusions:** TPe-SD was significantly higher in patients with LVH at rest and during exercise. TPe-SD was correlated with LV mass index and E/E′ at peak exercise.

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**P1009 | BEDSIDE**

**Increased circulating mesenchymal stem cells in patients with essential hypertension and left ventricular hypertrophy**


**Purpose:** Stem and progenitor cells are implicated in ventricular remodelling and have great clinical significance in many cardiovascular diseases. However, there are limited data regarding the involvement of mesenchymal stem cells (MSCs) in the pathophysiology of arterial hypertension. The aim of this study was to investigate the distribution of MSCs in patients with essential hypertension.

**Methods:** We included 24 patients with untreated essential hypertension and 19 healthy individuals. All subjects underwent a complete echocardiographic study. In addition, peripheral blood samples from all participants were immunostained with antibodies against the cell surface markers CD34, CD45 and CD90. Using flow cytometry, we measured MSCs as a population of CD45−/CD34−/CD90+ cells and also as a population of CD45−/CD34−/CD105+ cells. The resulting counts were translated into the % percentage of MSCs in the total cells of peripheral blood.

**Results:** Hypertensive patients were shown to have increased circulating CD45−/CD34−/CD90+ compared to controls (0.0069±0.0121% compared to 0.0495±0.0015%, respectively, p<0.001). No statistically significant difference in circulating CD45−/CD34−/CD105+ cells was found between hypertensives’ and normotensives’ peripheral blood (0.018±0.013% compared to 0.015±0.014%, respectively, p=0.53). Notably, CD45−/CD34−/CD90+ circulating cells were positively correlated with left ventricular mass index (LVMI) (r=0.515, p<0.001).

**Conclusions:** Patients with essential hypertension have increased circulating MSCs compared to normotensives, and the number of MSCs is correlated with LVMI. Our findings contribute to the understanding of the pathophysiology of hypertension and might suggest a future therapeutic target.

**Figure 1:** A: B: Non. LVH. C: D: LVH at rest and exercise.

**Conclusion:** Intraventricular diastolic dyssynchrony during exercise is significantly associated with the degree of LVH in hypertensive patients. And exaggerated diastolic dyssynchrony during exercise can deteriorate diastolic function and this result might explain the exertional dyspnea in hypertensive patients with LVH.
P1091 | BEDSIDE
Relationship between biochemical markers of cardiac remodelling and postexercise elevation of left ventricular filling pressure in arterial hypertension
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Purpose: Recent studies have demonstrated the usefulness of multibiomarker approach for risk stratification of patients with arterial hypertension. The biological markers reflecting cardiac hypertrophy, fibrosis and apoptosis correlate with systolic and diastolic function of left ventricle (LV). The tissue Doppler E/e’ ratio at rest is a powerful predictor of cardiac events in a hypertensive population. Exercise E/e’ is an important contributor to the development of heart failure. Our objective was to compare blood markers of cardiac remodelling among hypertensive patients with normal and elevated postexercise E/e’.

Methods: The study group was composed of 227 untreated hypertensive males (aged 51±8 years). All patients underwent 24-hour ambulatory blood pressure monitoring and conventional two-dimensional echocardiography. The E/e’ ratio measurement was performed before starting exercise and immediately after.

Results: All the patients had E/e’ ≤ 8 at rest. Fourteen patients (6.2%) presented postexercise elevation of LV filling pressure. Plasma carboxy-terminal propeptide of procollagen type I (PICP, a marker of cardiac fibrosis), cardiotophin-1 (CT-1, a marker of cardiac hypertrophy) and annexin V (a marker of apoptosis) were measured by ELISA.

Conclusions: Plasma PICP and annexin V levels were significantly higher in patients with elevated postexercise E/e’ (263.3 (102; 438.5) pg/ml vs. 140.8 (52.6; 192.3) pg/ml, p=0.047). Receiver operating characteristics curve analysis showed that a cut-off value of 140.8 pg/ml for the PICP provided 68% specificity vs. 103.5 (52.6; 192.3) pg/ml, p=0.047. Incremental AUC: 0.649, p=0.047). In ROC analysis, cfPWV emerged as a better predictor of L VMI levels (R2=0.243, B=1.60, p<0.001). In ROC analysis, cfPWV emerged as a better predictor of LVH (AUC: 0.735, p<0.001) compared to the FRS (AUC: 0.727, p<0.001), aortic systolic pressure (AUC: 0.687; p<0.001), aortic pulse pressure (AUC: 0.705; p<0.001) and AIX (AUC: 0.649, p<0.001).

Conclusions: Aortic stiffness is independently associated with LVH and is a better predictor of LVH than the FRS, aortic BPs and wave reflections. Elevated cfPWV significantly target organ damage, which extends beyond large artery stiffness and herald LVH. This has implications for risk stratification and choice of therapy.

P1093 | BEDSIDE
Visceral fat volume is associated with diastolic dysfunction in patients with resistant hypertension - Resist-POL Study
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Purpose: To evaluate the impact of obstructive sleep apnea and metabolic syndrome on left ventricle diastolic function in patients with resistant hypertension (RHT).

Methods: We analyzed data from 155 patients (92M, 63F). All patients underwent thorough examination including: biochemical evaluations (MS was defined by waist circumference ≥ 80 cm and blood pressure ≥ 140/90 mmHg), polysomnography (OSA was defined as apnoe/hypopnoea index ≥ 15/h) and echocardiography. Left ventricular mass index (LVMI) and diastolic parameters were obtained. Additional intravenous-adrenaline based vasodilatation study (VFV) was performed using L V filling pressure monitoring.

Results: Patients were divided into 4 groups based on presence of MS and OSA: group 1) OSA(−), MS(−) [n=42], group 2) OSA(−), MS(+) [n=14], group 3) OSA(+), MS(−) [n=46] and group 4) OSA(+), MS(+) [n=53]. There were no differences in L VMI and 24h SBP/DBP values between these groups. Table 1 shows variables of E/E’ and VFV. Both LVMI (r=0.36; p<0.0001) and VFV (r=0.40; p=0.002) correlated with E/E’. In a multivariate linear model including age, gender, AHI, 24-h SBP, 24-h DBP, LVMI and MS and AH were not independently associated with E/E’. In a multivariate linear model including age, gender, MS, 24-h SBP, 24-h DBP, LVMI and VFV independently associated with E/E’ were LVMI (beta=0.42, p<0.001) and VFV (beta=0.37, p<0.003).

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n=42)</th>
<th>Group 2 (n=14)</th>
<th>Group 3 (n=46)</th>
<th>Group 4 (n=53)</th>
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<tr>
<td>VFV</td>
<td>7.02±1.8</td>
<td>8.85±1.9</td>
<td>8.24±2.8</td>
<td>8.98±3.2</td>
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Conclusions: Among factors characterizing metabolic abnormalities the volume of visceral fat is most closely related with LV diastolic dysfunction in patients with true RHT.

P1094 | BEDSIDE
Development of LV hypertrophy in treated hypertensive patients: the Campania-Salute Network (CSN)
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Purpose: Left ventricular (LV) hypertrophy (LH) is the hallmark of hypertensive target organ damage and predictor of major cardiovascular (CV) events. In a population-based cohort, antihypertensive therapy might be less efficacious for regression of LH than indicated by results in clinical trials, independently of blood pressure (BP) control. We assessed whether both LH develops during antihypertensive treatment and a phenotype at risk is identifiable in a large cohort of treated hypertensive patients without LVH, referred to our tertiary care center.

Methods: From the Campania-Salute Network (CSN), we consecutively enrolled hypertensive patients (age 50±11 years, males 60%, baseline systolic pressure (SBP) 142±15 mmHg and diastolic BP (DBP) 90±10 mmHg), without echocardiographic LVH and prevalent CV disease, with glomerular filtration rate (GFR)>30 mL/min1.73m2, a follow-up of at least 1 year and a validated follow-up echocardiogram. Evaluation by echocardiography was done at the time of last clinical visit, LVMI was identified at LV mass index (LVMi)=50g/m2.7 in male patients and >47g/m2.7 in women.

Results: After a median follow-up of 56 months (inter-quartile range: 36-99), 457 patients (16%) had developed LHV. They were older, more often diabetic, with longer history of hypertension and more extended follow-up period (all p<0.001). They also exhibited higher baseline BMI and SBP, thicker carotid intima-media complex (IMT) and greater LVMi than patients without follow-up LHV (all p<0.001). SBP and DBP values were at 133±9, p<0.04. The last control was lower in patients developing LHV (both p<0.0001). No sex-difference was observed. During follow-up, patients developing LHV were prescribed more antihypertensive medications, and specifically more diuretics and Ca++-channel blockers (both
Conclusion: We demonstrated that LVH develops during antihypertensive therapy, despite more aggressive antihypertensive treatment. We identified a phenotype of hypertensive patient at high risk to develop LVH: elderly, overweight patients with isolated systolic hypertension and more LVMI close to cut-points and uncontrolled SBP despite aggressive therapy are likely to increase their LVMi over time to level of clear-cut LVH.

VASCULAR REMODELLING

P1097 | BENCH Muscle atrophy F-box (MAFbx) regulates neointimal formation during vascular remodeling in mice

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Purpose: Muscle atrophy F-box (MAFbx), also known as FBXO32, F-box protein 32 and atrogin-1, is an E3 ubiquitin ligase expressed only in muscle. MAFbx was originally identified as a critical mediator of skeletal muscle atrophy, and endogenous MAFbx plays an essential role in mediating pathological cardiac hypertrophy. However, the role of MAFbx in vascular remodeling remains unknown. In this study, we investigated the association between TNF-α and MAFbx and revealed the role of MAFbx in mediating a pathological form of vascular remodeling.

Methods and results: Mice were subjected to carotid artery ligation. After 4 weeks, expression levels of MAFbx mRNA were increased in the carotid artery. In cultured mouse vascular smooth muscle cells (MVMs), expression levels of MAFbx mRNA were confirmed and induced by TNFα-stimulation, TNFα-induced cell proliferation and migration in MVMs obtained from WT mice. Interestingly, these increases were significantly inhibited in MVMs obtained from MAFbx knockout (MAFbx-KO) mice. To evaluate the role of endogenous MAFbx during vascular remodeling, MAFbx-KO and WT mice were subjected to carotid artery ligation. After 4 weeks following this intervention, the intima/media ratio was significantly higher in WT mice than in MAF-KO mice (0.84±0.40 vs. 0.34±0.14, P<0.05). The expression levels of iκBα were reduced by TNFα for 30 min in MVMs obtained from WT mice. TNFα- induced attenuation of iκBα was reduced in MAFbx-KO mice as compared to WT mice. TNFα-also induced upregulation of iκBα in MVMs obtained from WT mice. These findings suggest that MAFbx might be a therapeutic target for preventing atherosclerosis and arterial restenosis after angioplasty.

P1098 | BENCH Factor VII activating protease (FSAP) deficiency promotes neointima formation by enhancing leukocyte accumulation and activity of matrix metalloproteinase-2 and -9

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Purpose: The factor VII activating protease (FSAP) is a multifunctional circulating plasma serine protease that also activates pro-urokinase. The Marburg I single nucleotide polymorphism (MI-SNP) in the FSAP-encoding gene is characterized by reduced FSAP activity associated with the formation of a null allele. The aim of this study was to determine the function of FSAP in vascular remodeling processes using mice lacking this gene.

Methods: Wire-induced injury of the femoral artery was performed to induce neointima formation in FSAP−/− mice on a C57BL/6 background and WT controls. Vessels were harvested 14 days after injury and were analysed by immunohistochemistry (IHC), qPCR, western blotting and quantitative zymography. In vivo microscopy was performed on the mouse cremaster muscle to analyse leukocyte recruitment to the perivascular tissue upon 4 hours of stimulation with chemokine (C-C motif) ligand 2.

Results: The neonatal lesion size and the proliferation of vascular smooth muscle cells were significantly enhanced in FSAP−/− mice compared to WT controls.
I interferons have been identified as proatherosclerotic cytokines and in mouse with insufficient coronary collateral growth (i.e. arteriogenesis). Furthermore, increased interferon-beta (IFN-β) concentration tested (10^{-5}M) was not observed on COX-1 and ICAM-1 protein in either cell type. Ticagrelor compared to CAM decreased VCAM-1 expression in a concentration-dependent manner in HAECs and HBMVECs. Tal eNOS levels were not altered. CAM treatment did not affect eNOS activation. TF expression in a concentration-dependent manner in HAECs and HBMVECs. Ticagrelor, unlike CAM showed anti-coagulant properties by reducing some of the beneficial effects may be mediated in a platelet- or even P2Y12 receptor-independent manner.

Methods: To investigate potential endothelium dependent effects of P2Y12 antagonists, primary human aortic- (HAECs), brain microvascular- (HBMVECs) and carotid bifurcations-endothelial cells (HCMECs) were stimulated with TNFα (10 ng/ml) and treated with increasing concentrations of clopidogrel-active metabolite (CAM) (1.5x10^{-6}M–1.5x10^{-5}M), which binds to the P2Y12 receptor after CYP 450 activation or ticagrelor (10^{-5}M–10^{-7}M). Effects of anti-platelet drugs on endothelial activation was determined by expression of pro-coagulant tissue factor (TF) and its counter-player TF pathway inhibitor (TPII), expression and activity of eNOS, expression of COX-1, COX-2 and the adhesion molecules VCAM-1 and ICAM-1 by western blotting. Additionally, underlying signal transduction pathways were assessed. The expression of P2Y12 receptors was investigated by qRT-PCR and cell-specific role for adenosine receptor activation of eNOS. The effects were observed before or after non coronary interventions.

Results: Ticagrelor, unlike CAM showed anti-coagulant properties by reducing TF expression in a concentration-dependent manner in HAECs and HBMVECs but not HCMECs. The observed effect was mediated via P2Y13 and P7056 kinase. Further, activation of eNOS by phosphorylation (Ser1177) was increased by ticagrelor via P13 kinase in HAECs but not in microvascular ECs, whereas total eNOS levels were not altered. CAM treatment did not affect eNOS activation in any cell type. Ticagrelor compared to CAM decreased eNOS expression and augmented COX-2 protein levels via the MAP Kinase pathway at the highest concentration tested (10^{-5}M). No effect was observed on COX-1 and ICAM-1 protein levels. Surprisingly, P2Y12 receptor mRNA was not detected in endothelial cells. Furthermore, pre-incubation of cells using specific adenosine receptor antagonists did not affect the effects of ticagrelor.

Conclusions: Ticagrelor, unlike CAM displays 1) an anti-coagulant and anti-inflammatory profile and 2) enhances activation of eNOS. The effects were observed to be cell-specific and appeared to be mediated independently of P2Y12 or adenosine receptors. These findings may have additional implications for ticagrelor in cardiovascular disease.

P1100 | BENCH
A monoclonal antibody against the interferon-alpha/beta receptor subunit 1 stimulates arteriogenesis in a murine hindlimb-ischemia model without affecting atherosclerosis

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Background: Increased interferon-beta (IFNβ) signaling was shown in patients with insufficient coronary collateral growth (i.e. arteriogenesis). Furthermore, mice treated with IFNβ demonstrate inhibition of arteriogenesis. Interestingly, type I interferons have been identified as proatherosclerotic cytokines and in mouse models of atherosclerosis, IFNβ treatment accelerated lesion formation and increased accumulation of macrophages in plaques. We hypothesized that monoclonal antibodies inhibiting IFNβ signaling will stimulate arteriogenesis and at the same time attenuate atherosclerosis.

Methods: In a murine hindlimb-ischemia model, atherosclerotic apolipoprotein E (APOE)−/− and low density lipoprotein receptor (LDLR)−/− mice were treated respectively during a 1- and 4-week period with blocking monoclonal antibodies (mAbs) specific for mouse Interferon-α/β Receptor subunit 1 (IFNAR1) or murine IgG isotype as control. The arteriogenic response was quantified using laser Doppler perfusion imaging of plugging (LDPI) as well as immunohistochemistry. Effects on atherosclerosis were determined by quantification of plaque area and composition analysis by immunohistochemistry. Several downstream targets of IFNβ were assessed by real time polymerase chain reaction (RT-PCR), both in the aortic arch as well as in hindlimb muscle.

Results: Hindlimb perfusion restoration after femoral artery ligation was improved in mice treated with anti-IFNAR1 compared to controls as assessed by LDPI. This was accompanied by a decrease in CXCL10 expression in the IFNAR1 MAb treated group. Anti-IFNAR1 treatment reduced plaque apoptosis without affecting total plaque area or other general plaque composition parameters.

Conclusion: Blocking IFNAR1 using monoclonal antibodies during 1- and 4-week treatment periods stimulates collateral artery growth in mice without exacerbating atherosclerosis. This is the first reported successful strategy using monoclonal antibodies to stimulate arteriogenesis.

P1101 | BENCH
Long-term performance of autologous tissue ultra-small-caliber vascular grafts (biotubes) in a rat abdominal aorta replacement model

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Objective: There are practically no small-caliber synthetic vascular grafts (<6 mm) with acceptable patency rate for the use of coronary bypass or peripheral vascular repair below the knee. We have developed autologous small-caliber vascular grafts, named "biotubes", by simple, safe and economical "in-body tissue architecture technology", which is a novel concept of regenerative medicine and one of the in vivo tissue engineering. In this study, we evaluated the long-term (more than 1 year) results of ultra-small-caliber biotubes using a rat abdominal aorta replacement model.

Methods: Silicone rod molds (diameter: 1.5 mm, length: 20 mm) were placed into subcutaneous pouches of rats, and after 1 month the implants with their surrounding connective tissues were removed. Biotubes with internal diameter of 1.5 mm were obtained as tubular connective tissues from the implants after pulling out the impregnated molds. After anti-thrombogenic coating, they were auto-implanted to the infrarenal abdominal aorta using an end-to-end anastomosis. At over 1 year (14-18 months, median 16 months), graft status was evaluated by ultrasonography, 7-tesla magnetic resonance angiography (MRA) and histology.

Results: High patency rate of 83% (10/12) was obtained. During observation period, ultrasonography and MRA showed little stenosis, no aneurismal dilation in biotubes, and no anastomotic intimal hyperplasia. Their luminal surface was smooth and completely covered with endothelial monolayer.

Conclusion: Long-term implantation results of ultra-small caliber biotubes were firstly reported. The biotubes performed as excellent vascular grafts with high patency and regeneration activity including complete endothelialization without aneurismal formation, stenosis.

Figure 1. Biotube implantation.

Conclusions: These beneficial effects of FSAP provide a direct mechanistic explanation for the observations in human disease.
heart disease in adult. Cardiac computed tomography (CT) is known as an excellent tool for evaluating congenital heart disease including ASD. The purpose of this study was to investigate the usefulness of cardiac CT in evaluating the morphology and hemodynamics of secundum ASD in adult using a new software, compared with transthoracic echocardiography (TTE), transesophageal echocardiography (TEE) and invasive catheterization.

Methods: A total of 50 patients (60±14 years old, 64% female) with secundum ASD were enrolled. Cardiac CT was performed, followed by 3D reconstruction of ASD for determination of the defect size, the length of rims from the circumference of ASD and the pulmonary to systemic blood flow ratio (Qp/Qs) in the Siemens workstation (syngo.CT Cardiac Function and RVA-Right Ventricular Volumetry), results were compared among TEE, TTE, invasive catheter and CT measurement.

Results: Cardiac CT was comparable with TTE and TEE in evaluating Qp/Qs as a reference standard of invasive catheterization (r=0.786; p<0.001, r=0.731; p<0.001, respectively). A linear association was observed between cardiac CT and TEE in evaluating ASD size (r=0.961; p<0.001). The length of rims from the circumference of ASD evaluated with cardiac CT were also comparable with those with TEE, the rim length from aortic valve (r=0.925; p<0.001), mitral valve (r=0.916; p<0.001), tricuspid valve (r=0.867; p<0.001), inferior vena cava (r=0.966; p<0.001) and posterior of atrium (r=0.884; p<0.001).

Conclusion: Cardiac CT is of use in evaluating the Qp/Qs, size of ASD and the length of rims from the circumference of ASD. Cardiac CT could be informative modality for optimizing clinical management for ASD patients.

P1104 "BEDSIDE" CT sizing of left atrial appendage prior to percutaneous closure using watchman device: feasibility and initial experience

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Purpose: Percutaneous interventional closure of the left atrial appendage (LAA) using the Watchman device (Boston scientific, Natick, Massachusetts) has emerged as an alternative therapy for reduction of embolic stroke in patients with non-vascular atrial fibrillation and contraindications to oral anticoagulation. Device sizing is based on TEE as well as angiographic measurements. Computed tomography (CT) provides complete volumetric evaluation of the LAA. We assessed the feasibility of CT sizing of the LAA prior to closure using the Watchman device.

Methods: 13 patients referred for interventional LAA closure were examined using Dual Source CT prior to the interventional procedure. Data sets were acquired using prospectively ECG-triggered high pitch spiral acquisitions triggered at 60% of the cardiac cycle. Multiplanar reconstructions were aligned with the plane of the LAA ostium and measurements were performed in a cross-sectional plane orthogonal to the long axis of the LAA at the level of the left circumflex coronary artery. Three measurements were performed: mean diameter (maximum + minimum diameter/2), effective diameter from area measurement (\(\sqrt{area/\pi}\)) x 2) and effective diameter from perimeter measurement (perimeter/\(\pi\)). LAA dimensions determined by CT were compared to intraprocedural sizing, which was based on angiographic and TEE assessment.

Results: Mean patient age was 76±7 years (8 males). LAA closure was successfully performed in all 13 patients with no relevant leak (2x33 mm, 5x27mm, 4x42mm and 3x21mm device). In one patient 2 devices (1x33mm and 1x21mm) were used due to a very wide LAA ostium. Mean diameter, perimeter derived effective diameter and area derived effective diameter as determined by CT were not significantly different (23±5 mm, 23±5 cm and 22±5 cm, respectively, p=0.9). Agreement between CT sizing and initial intra-procedural sizing was slightly better for mean diameter and perimeter derived effective diameter (8/13) compared to area derived effective diameter (7/13). Initial intraprocedural sizing was changed in 3 patients due to failed implantation (upgraded in 2 patients and downgraded in 1 patient). In patients with disagreement between intraprocedural sizing and the 3 CT-based measurements, CT recommended a smaller device in 3 patients and a larger device in 1 patient, and the device was implanted according to the intraprocedural sizing.

Conclusions: CT sizing of the LAA prior to interventional closure is feasible. Whether CT-based sizing would correlate to better interventional or clinical outcomes needs to be further evaluated.

P1105 "BEDSIDE" Feasibility of an ultra low dose CT for left atrium and pulmonary veins imaging using a new model-based iterative reconstruction

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Purpose: To evaluate the feasibility of ultra low dose CT for left atrium and pulmonary veins imaging using new model-based iterative reconstruction

Materials and methods: 200 patients, with persistent or intermittent atrial fibrillation, scheduled for catheter ablation were enrolled in this study and randomized into two groups: Group 1 (100 patients, MDCT with VEO, no ECG triggering, tube voltage and tube current of 100kV and 60 mA, respectively, regardless of patient’s BMI) and Group 2 (100 patients, MDCT with adaptive statistical iterative reconstruction algorithm (ASIR) rather than MBIR, no ECG-triggering and, KV and mA tailored on patient BMI). The image quality, the CT-attenuation, image noise, signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR) of left atrium and every pulmonary vein branch and Effective Dose (ED) were evaluated for each exam and compared between two groups.

Results: No differences between two groups in terms of population characteristics and image quality score. Statistically significant differences were found between Group 1 and Group 2 in mean attenuation, SNR, and CNR of left atrium. Significant lower values of noise were found in Group 1 vs Group 2 in the quantitative analysis of pulmonary veins. Group 1 showed a significantly lower mean ED in comparison with Group 2 (0.49±0.03 versus 6.01±2.2 mSv).

Conclusions: The CT for left atrium and pulmonary veins imaging using VEO is feasible and allows to perform examinations with very low radiation exposure without loss of image quality

P1106 "BEDSIDE" Pre-procedural planning for percutaneous left atrial appendage occlusion using 3-dimensional patient-specific models obtained by 3D printing: a proof-of-concept analysis

M. Wu1, J. Makaryus2, A. Makaryus1, A. Patel1, B. Goldner1, D.J. Slotwiner1.

1Long Island Jewish Medical Center, Cardiology, New Hyde Park, United States of America; 2Columbia University Medical Center, New York, United States of America

Purpose: To evaluate the feasibility of ultra low dose CT for left atrium and pulmonary veins imaging using new model-based iterative reconstruction

Materials and methods: 200 patients, with persistent or intermittent atrial fibrillation, scheduled for catheter ablation were enrolled in this study and randomized into two groups: Group 1 (100 patients, MDCT with VEO, no ECG triggering, tube voltage and tube current of 100kV and 60 mA, respectively, regardless of patient’s BMI) and Group 2 (100 patients, MDCT with adaptive statistical iterative reconstruction algorithm (ASIR) rather than MBIR, no ECG-triggering and, KV and mA tailored on patient BMI). The image quality, the CT-attenuation, image noise, signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR) of left atrium and every pulmonary vein branch and Effective Dose (ED) were evaluated for each exam and compared between two groups.

Results: No differences between two groups in terms of population characteristics and image quality score. Statistically significant differences were found between Group 1 and Group 2 in mean attenuation, SNR, and CNR of left atrium. Significant lower values of noise were found in Group 1 vs Group 2 in the quantitative analysis of pulmonary veins. Group 1 showed a significantly lower mean ED in comparison with Group 2 (0.49±0.03 versus 6.01±2.2 mSv).

Conclusions: The CT for left atrium and pulmonary veins imaging using VEO is feasible and allows to perform examinations with very low radiation exposure without loss of image quality

P1108 "BEDSIDE" Cardiac CT measurements in evaluating ASD.

Conclusion: Cardiac CT is of use in evaluating the Qp/Qs, size of ASD and the length of rims from the circumference of ASD. Cardiac CT could be informative modality for optimizing clinical management for ASD patients.
thromboemboli arising from the morphologically diverse left atrial appendage (LAA). We demonstrate the feasibility of a priori LAA 3D model analysis using cardiac CT and cost-effective commercially available 3D printing for pre-procedural modeling of the LAA.

Methods: The 320-slice cardiac CT exams of six random patients were selected serving as source data. CT DICOM data was converted to stereolithography (STL) files (Simpleware, LTD). The MakerBot Replicator 2X was employed as the consumer level 3D printer and compared with Stratasys™ Objet500 Connex which served as the reference professional-grade printer. The MakerBot prints were created using poly lactic acid (PLA) filament. The Stratasys prints were created using proprietary material.

Results: Six different LAA replicas were produced using each printer. The prints from both models were equivalent in fidelity of reproduction, level of detail, and quality of print. Print times were similar, averaging between 90-120 minutes. The cost of the Stratasys ($over $1000) and TangoPlus® (approximately $2/inch2) is substantially greater than the MakerBot Replicator 2 ($2500) and PLA filament (less than $0.10 per model). Using the TangoPlus material and Stratasys produced rubber-like prints which are more amenable to simulation of surgical procedures and for training purposes. The firm characteristics of the PLA prints are more durable and suited for making measurements to size LAA occlusion devices. The biggest hurdle in the process was learning how to use the software. After the initial learning curve, DICOM images could be transformed into 3D models within about 1 hour.

Conclusion: This proof-of-concept analysis has demonstrated the feasibility of using cost-effective and readily available commercial-grade 3D printing technology to accurately recreate the LA and LAA prior to intervention. We believe that safety, efficacy, and patient education regarding LAA occlusion procedures will be aided by pre-procedural visualization, tactile manipulation, measurement, and sizing of equipment using 3D printing.

P1108 | BEDSIDE
Diagnostic performance of cardiac CT in detecting left atrial thrombus
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Purpose: The exclusion of left atrial thrombus is essential before the electrical- or pharmacological cardioversion in patients with atrial fibrillation. In clinical practice transoesophageal echocardiography (TEE) is the reference standard method to diagnose left atrial thrombus. We aimed to evaluate the diagnostic performance of cardiac computed tomography angiography (CTA) regarding the detection of left atrial thrombus compared to the gold standard TEE.

Methods: In total 444 patients were referred to left atrial angiography before atrial fibrillation ablation procedure (149 women, 295 men, mean age 56y) between February 2011 and January 2014. We have investigated the patients who subsequently underwent TEE (n=201).

Results: CTA excluded left atrial thrombus in 178 cases. In all negative CTA cases were confirmed by TEE (true negatives). In 23 cases CTA showed incomplete contrast filling in the left appendage: 19 false positives and 4 true positives. According to our results sensitivity of cardiac CT is 100% [95% CI: 40.2%-100%], specificity was 90.4% [95% CI: 85.4%-94.1%], negative predictive value was 100% [95% CI: 97.9%-100%] and positive predictive value was 17.4% [95% CI: 5.1%-38.8%].

Conclusion: Cardiac CT is a very sensitive modality diagnosing left atrial thrombus, the negative predictive value proved to be 100%. In patients where cardiac CTA excludes left appendage thrombus subsequent TEE examination may be unnecessary.

PROGNOSIS IN HEART FAILURE: SCIENCE AND UNCERTAINTIES

1124 | BEDSIDE
Steep decline in mortality from heart failure over three decades
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Purpose: The proportion of deaths due to heart failure (HF) reflects both its prevalence and survival. Prevalence of HF is increasing, but survival is longer. Selection rules for assigning the underlying cause of death discourage the selection of HF as a cause of death if other causes are certified on the same death certificate. We sought to define trends in population mortality attributable to HF in a national population and a large regional population, using all certified causes of death, not just underlying cause.


Results: HF was mentioned as a factor contributing to death in 310,594 cases between 2001–10 in England. Mortality rates based on underlying cause alone underestimated the impact of HF on overall population mortality (compared to those based on all recorded causes of death) by a factor of six. Analysing all mentions of heart failure, we found that mortality rates from HF have declined dramatically over the last 30 years. Considering all ages and both sexes combined, age- and sex-standardised mortality measured as all recorded causes of death in 2008–10 were only 40% of those in 1981–83.

Conclusion: Mortality rates based on underlying cause are a more sensitive marker of the contribution of HF to overall population mortality. There have been very substantial declines in the population mortality of HF, with the decline beginning well before the introduction of modern medical and device therapy for the condition.
1125 | BEDSIDE
Is there a heart rate paradox in acute heart failure?

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Background: Higher heart rate (HR) associates with higher mortality in chronic heart failure (HF). The impact of HR in acute HF is not established. We studied the prognostic impact of admission HR in patients hospitalized due to acute HF and analyzed if prognostic implications differed between patients admitted in sinus rhythm (SR) and those in atrial fibrillation (AF).

Methods: Patients admitted with acute HF were prospectively included. Clinical data, laboratory parameters and co-morbidities were recorded. An echocardiographic examination was performed. Physicians were aware of the ongoing registry. Primary endpoint was all-cause death. Follow-up was 6 months. We used a Cox regression analysis to study the association of HR with 6-month all-cause mortality. HR was analyzed both as a continuous variable and as a categorical variable: <100 and ≥100 beats per minute (bpm). Analysis was stratified according to admission rhythm. Multivariate models were built. Cross classification was made according to admission (cut-off 100 bpm) and discharge (cut-off 80 bpm) HR and association with outcome determined.

Results: We analyzed 577 patients. Median age was 78 years, and 56.6% had left ventricular systolic dysfunction. Median emergency department HR was 86 (72-101) bpm, 258 were in AF. During follow-up 112 patients died. Death risk increased steadily with lower admission HR. The association of HR with mortality was significant only in patients in SR. Patients with an admission HR >100 bpm had a hazard ratio (95% CI) of death at 6 months of 4.76 (1.71-13.21) when in SR and 1.56 (0.87-2.79) when in AF. Association was independent of systolic blood pressure, New York Heart Association class, B-type natriuretic peptide, age, ischaemic aetiology, systolic dysfunction, prognostic modifying therapy and hemorrhage rate. The multivariate adjusted hazard ratio of 6-month death in patients in SR with HR >100 bpm was 2.92 (1.02-8.34). Per each 10 bpm increase in HR the multivariate adjusted hazard ratio was 0.82 (0.68-0.98). Ninety-three patients had admission HR >100 and discharge HR >80 bpm; 286 admission HR <100 and discharge HR >80 bpm and 120 admission HR >100 and discharge HR >80 bpm; mortality rates at 6-months were 8.6%, 14.1%, 21.4% and 26.7%, p=0.004.

Conclusions: In acute HF patients in SR, those presenting with tachycardia have a better outcome. Per each 10bpm increase in admission HR there is a 18% decrease in 6-month death risk. This association with prognosis is not observed in AF. Patients presenting with tachycardia and discharged with controlled HR have the better outcome.

1126 | BEDSIDE
Benefit of positive airway pressure (PAP) therapy in patients with sleep apnoea (SA) in Germany: a retrospective comparative cohort analysis based on a statutory health insurance (SHI) database

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Purpose: SA is relatively common, occurring in about 20% of adult males and 10% of females. This study investigated the effects of PAP therapy on morbidity (including comorbid disease), all-cause and disease-specific mortality, and costs in patients with SA in Germany from a SHI perspective.

Methods: Outcomes for a total of >4 million individuals covered by the SHI database were analysed (approximately 5% of the German SHI population). PAP therapy was initiated in 4068 patients with SA. Propensity score was used to define a control group of 4068 SA patients matched for age, sex, risk factors/etiology, region and medication who received usual care (no PAP). Patients were followed over three years after initiation of PAP.

Results: Mean patient age was 60 years, and 80% of patients were male. Baseline patient characteristics were similar in the PAP and no PAP groups, except for obesity (significantly more common in the PAP group, 33.84% vs 27.11%; p<0.0001). The three-year mortality rate was significantly lower in patients treated with PAP compared with the no PAP group (4.5% vs 7.2%, 37.5% reduction; p<0.0001). Three-year rates for coronary heart disease mortality (4.5% vs 7.2%, 37.5% reduction; p<0.0001) and heart failure mortality (14.7% vs 21.4%, 31.6% reduction; p=0.0001) were also significantly lower in the PAP vs no PAP group.

Conclusion: PAP therapy for patients with SA significantly reduced three-year mortality compared with usual care.

1127 | BEDSIDE
Atrial fibrillation and the risk of incident heart failure in community-dwelling older adults: findings from a propensity-matched cohort of a prospective population study

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Background: Atrial fibrillation (AF) is common in older patients with heart failure (HF) and is considered a risk factor for HF. However, to what extent this association is independent remains unclear. The objective of the current analysis was to examine the impact of AF on incident HF in a propensity-matched cohort from a community-dwelling population of older adults without HF.

Methods: Of the 5795 community-dwelling adults aged >65 years in the Cardiovascular Health Study (CHS), 5521 were free of prevalent HF at baseline, of which 116 had ECG-documented AF at baseline. Propensity scores for AF, calculated for each participant, were used to assemble 114 pairs of those with and without AF who were balanced on 30 baseline characteristics. Cox regression analysis based on a propensity-matched association of AF with centrally adjudicated HF over 13 years of follow-up.

Results: Participants (n=228) had a mean (±SD) age of 75 (±6) years, 41% were women, and 6% were African American. Incident HF occurred in 45% and 24% of matched participants with and without AF, respectively during 13 years of follow-up (HR, 2.13; 95% CI, 1.36–3.46; p=0.001; Figure 1). Baseline AF had no association with all-cause mortality (HR, 1.07; 95% CI, 0.77–1.48; p=0.687).

Figure 1. KM plots for incident heart failure by atrial fibrillation.

Conclusion: Among community-dwelling older adults, baseline AF is an independent risk factor for incident HF but had no independent association with mortality.

1128 | BEDSIDE
Efficacy and safety of ticagrelor in patients with acute coronary syndrome and heart failure - insights from the platelet inhibition and patient outcomes (PLATO) trial

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Purpose: Heart Failure (HF) is a frequent complication of patients with acute coronary syndromes (ACS). We examined the efficacy and safety of ticagrelor in patients with ACS and HF as well as evaluated baseline predictors of post-discharge HF in ACS patients.

Methods: We classified all 18,624 patients with ACS in the PLATO trial in two groups - ACS and HF. All participating hospitals used ticagrelor in ACS patients. The primary endpoint was a composite of death, myocardial infarction, resuscitated cardiac arrest, and stroke. ACS and HF patients were propensity score-matched with a 1:1 ratio to assess differences in the primary endpoint.
groups; no HF and HF based on the presence of clinical signs of HF (on admission, in-hospital or post-discharge), NT-proBNP > 2500 pmol/mL, or Killip class II or III on admission. We used Cox-regression models with HF as a time-dependent variable to evaluate efficacy of ticagrelor versus clopidogrel on clinical endpoints and safety. In patients without prior HF at the time of hospital discharge, a multivariable Cox regression model was used to assess predictors of post-discharge HF.

Results: Overall, a total of 3324 (17.8%) patients experienced HF following the ACS index event. Patients with HF were older, more often female and with significantly more co-morbidities than patients without HF. Patients randomized to ticagrelor, compared to clopidogrel, experienced lower risk of efficacy clinical events regardless of the presence of HF. The risk of bleeding was similar between the two groups. A total of 990 patients experienced HF after hospital discharge (2.24% at 6 months, and 3.96% at 12 months). Predictors of developing post-discharge HF were: higher heart rate, higher NT-proBNP, troponin I > 0.08μg/mL, hypertension, chronic obstructive pulmonary disease and older age.

Conclusion: We found clinical predictors for post-discharge HF that may guide treatment strategies in patients with ACS. Ticagrelor significantly decreased mortality in ACS patients, without causing more major bleedings, compared with clopidogrel regardless the presence of HF.

1129 | BEDSIDE
Myocardial fibrosis in patients with non-ischemic cardiomyopathy compared to established prognostic factors
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Purpose: The study sought to compare the prognostic value of myocardial fibrosis to other clinical, laboratory, electrocardiographic and echocardiographic findings in patients with non-ischemic cardiomyopathy (NICM).

Methods: 283 NICM patients referred to a tertiary Centre underwent clinical examination, plasma N-terminal fragment of probrain natriuretic peptide (NT-proBNP) assay, electrocardiography, echocardiography, Holter monitoring and cardiac magnetic resonance for late gadolinium enhancement (LGE) detection and quantification. All patients were then followed-up for a 32-month median period (interquartile range 18-50) for a composite end-point including cardiac death, hospitalization for heart failure and aborted sudden cardiac death.

Results: LGE was detected in 135 (48%) patients. 91 (32%) patients achieved the study end-point. At multivariate analysis, higher NT-proBNP concentrations (HR: 1.269 [1.012-1.585], P:0.039) and LGE presence (HR: 2.035 [1.212-3.414], P:0.007) or greater extent (HR: 1.092 [1.011-1.179], P: 0.024) were associated with high likelihood of achieving the combined end-point, independently of other prognostic determinants, including New York Heart Association (NYHA) functional class, left ventricular ejection fraction (EF), right ventricular EF, left atrial area, mitral regurgitation, and non-sustained ventricular tachycardia episodes at Holter monitoring.

Conclusions: In NICM patients, myocardial fibrosis is a strong and independent predictor of adverse outcome, when compared to other established prognostic markers.

1130 | BEDSIDE
Frailty is related with decreased survival in elderly patients hospitalized with heart failure
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Purpose: To evaluate the frailty phenotype influence on survival of elderly patients with heart failure and relation of frailty with ejection fraction of daily activities.

Methods: One-year follow-up prospective study of 431 consecutive patients. We included patients older than 74 years with high comorbidity who were admitted with a main diagnosis of decompensated heart failure. Clinical characteristics, including geriatric assessment, were recorded during index admission; post-discharge follow-up included frailty assessment by Fried et al criteria (grip strength, gait speed, physical activity, fatigue and unintentional weight loss). The relationship among frailty status and survival was analysed trough Kaplan-Meier survival curves in frail and non-frail patients and Cox regression analysis adjustment for covarates.

Results: Mean age was 85±5 years, 59.7% were females, mean Charlson co-morbidity index was 3.1±1.8; basal NYHA functional class III-IV was present in 28.7% of patients. Forty three percent of patients had a previous admission during the last 9 months. 33% showed atrial fibrillation on admission. Left ventricle ejection fraction was lower than 45% in 20.2% of patients. Treatment on discharge included ACEI or ARB in 58.6% and beta-blocker in 34%. Dependence in any ADL was present in 43.7% of patients and 41% fulfilled frailty criteria.

One-year mortality was 27% in frail patients and 15% in non-frail patients (p<0.03). Frailly non-adjusted for HR for mortality was 1.99 (95% CI 1.25-3.17). On a multivariate parsimonious model (Cox regression), frailty (HR 1.74, 95% CI 1.08-2.79), age (HR 1.07 per year, 95% CI 1.02-1.12), dementia (HR 3.08, 95% CI 1.56-6.06), serum creatinine (HR 1.43 per mg/dl, 95% CI 1.04-1.96), preserved ejection fraction (HR 0.52, 95% CI 0.32-0.85) were independently related with mortality. On a multivariate non-parsimonious model (Cox regression), including previous variables and gender, beta-blocker treatment, ACEI-ARB treatment and potassium-sparing agents treatment, frailty (HR 1.64, 95% CI 1.01-2.68) was independently related with mortality.

Conclusions: Frailty phenotype is independently related with one-survival in elderly patients admitted with heart failure. Identification of frailty should be included in these patients' assessments as can identify high risk cases that deserve more extensive diagnostic and therapeutic interventions. Frailty is also relevant in these clinical trials since can determine survival as a covariate. Simple measures of frailty, such as gait speed or grip strength should be evaluated as clinical practice in cardiology.

1131 | BEDSIDE
A potential linkage between mitochondrial function of the heart and leg muscle in patients with heart failure
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Purpose: Congestive heart failure (CHF) often accompanies cachexia, namely body wasting, which is a potential target of therapeutic intervention in cases of CHF. To gain insight into the mechanism of cardiac cachexia, we hypothesized that patients with chronic heart failure (CHF) would show the impairment in mitochondrial function of legs along with the decrease of legs activity. Mitochondrial activity is measured by electron transport system (ETS) and metabolic parameters in clinical trials since can determine survival as a covariate. Simple measures of frailty, such as gait speed or grip strength should be evaluated as clinical practice in cardiology.

1132 | BEDSIDE
Lower activation of renin-aldosterone and sympathetic nervous systems in overweight patients with acute heart failure and its association with favorable short-term prognosis

Background: Previous studies have demonstrated that higher body mass index (BMI) was associated with better prognosis in the setting of heart failure, so called “obesity paradox”. The underlying mechanisms of the obesity paradox have not yet been determined, but hormonal response to haemodynamic alteration could explain it. We have postulated that adipose tissue can be a hormone-producing organ. We prospectively enrolled patients admitted for acutely decompensated heart failure (ADHF), and sought to examine activation of renin-aldosterone and sympathetic nervous systems in overweight patients in association with favorable short-term clinical outcome.

Methods and results: A total of 281 consecutive ADHF patients (183 men; mean age 76±12 years) admitted to our hospital was studied. Patients were divided into two groups according to BMI; overweight patients, BMI ≥30kg/m²; and normal weight patients, BMI <30kg/m². The overweight group was significantly higher in age (p<0.001), creatinine (p<0.001), systolic blood pressure (p<0.001), and heart rate (p<0.001). Plasma renin activity, plasma aldosterone concentration, and plasma norepinephrine concentration were measured both on admission and discharge and plasma renin activity, plasma aldosterone concentration, and plasma norepinephrine concentration were measured both on admission and discharge.
before discharge. Overweight patients were associated with younger age, higher serum Na level, lower plasma BNP level, and higher hemoglobin level. Medications including ACE inhibitors/ARB, β-blockers, and aldosterone antagonists were not different between overweight and lean subjects. Despite that systolic blood pressure on admission was greater (140.2±7 vs. 131.1±3 mmHg, P=0.028), the overweight group, as compared with the lean group, had lower plasma renin activity (4.1±1.5 vs. 7.1±1.2 ng/mL/hr, P=0.049), plasma aldosterone concentration (83.5±77 vs. 126.6±140 pg/mL, P=0.016), and plasma noradrenaline level (568±368 vs. 801±922 pg/mL, P=0.049) on admission. However, those values were comparable in both groups before discharge. Multivariate Cox proportional hazard regression analysis showed BMI ≥25 kg/m² was independently associated with a lower adverse events (OR: 0.15, p<0.01) among variables including sex, age, history of hypertension and diabetes mellitus, serum Na and creatinine levels, plasma BNP level, and left ventricular ejection fraction.

Conclusions: Overweight patients showed better short-term prognosis compared to lean patients. Lower activation of renin-aldosterone and sympathetic nervous systems at acute phase of decompensation was shown in overweight patients, suggesting one of the underlying mechanisms for the obesity paradox.

1133 | BEDSIDE
Prognostic impact of metabolic syndrome in patients with chronic heart failure: a result from GISSI-HF trial
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Purpose: Prognostic role of Metabolic Syndrome (METS) in unselected populations and in patients with CHD has been defined previously. We evaluated the impact of METS on prognosis in chronic heart failure (HF).

Methods: International Diabetes Federation criteria were used for METS. Adjusted Cox's regression models with total mortality and death for HF worsening as outcomes were fitted in 6,648 patients (pts) enrolled in GISSI-HF trial with no missing values for the variables of interest. Impact of each component of METS on prognosis was also assessed.

Results: See Table. METS compared to no METS was significantly associated with risk of total and HF death. As compared with pts with METS and no type 2 DM, the risks of total and HF death were significantly lower in patients with METS and no DM, whereas they were significantly increased in pts with DM and no METS. Pts with METS and DM showed no difference as to risk of total and HF death compared with pts with no METS and no DM. Risk of total and HF death were lower in pts with BMI ≥30 or hypertension (SBP ≥140 or DM or low HDL-C (≤40mg/dl in males and ≤50mg/dl in females). No association was found between METS and triglycerides (≥150mg/dl).

Conclusions: In HF, METS is associated with lower total and HF death. Such findings are likely due to reverse epidemiology.

NOVEL BIOMARKERS IN PREDICTING CARDIOVASCULAR DISEASES

1134 | SPOTLIGHT
The biomarker tissue inhibitor of metalloproteinase-1 (TIMP-1) is an independent predictor of all-cause mortality in the AGES-Reykjavik study
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Purpose: Biomarkers matlproteinease-9, (MMP-9), and tissue inhibitor of metalloproteinase-1 (TIMP-1), relate to remodeling of the extracelular matrix.

Abstract Table 1

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>All-cause mortality</th>
<th>P</th>
<th>Death for HF worsening</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>METS+ (1,212 pts, 18.2%)</td>
<td>261 (21.5)</td>
<td>0.83 (0.72–0.95)</td>
<td>0.005</td>
<td>73 (6.0)</td>
</tr>
<tr>
<td>METS- (5,436 pts, 81.8%)</td>
<td>1619 (27.9)</td>
<td>1.00 (ref.)</td>
<td>-0.0001</td>
<td>546 (10.0)</td>
</tr>
<tr>
<td>METS-DM+ (1,651 pts, 24.8%)</td>
<td>619 (37.5)</td>
<td>1.34 (1.21–1.48)</td>
<td>-0.0001</td>
<td>222 (13.4)</td>
</tr>
<tr>
<td>METS-DM+ (665 pts, 10%)</td>
<td>170 (25.6)</td>
<td>1.03 (0.87–1.21)</td>
<td>0.762</td>
<td>50 (7.5)</td>
</tr>
<tr>
<td>METS-DM- (457 pts, 8.2%)</td>
<td>91 (16.6)</td>
<td>0.76 (0.62–0.95)</td>
<td>0.015</td>
<td>23 (4.2)</td>
</tr>
<tr>
<td>METS-DM- (3,785 pts, 56.9%)</td>
<td>994 (26.3)</td>
<td>1.00 (ref.)</td>
<td>0.01</td>
<td>324 (8.6)</td>
</tr>
<tr>
<td>BMI ≥30 (1,492 pts, 22.4%)</td>
<td>331 (22.8)</td>
<td>0.85 (0.76–0.96)</td>
<td>0.011</td>
<td>97 (6.5)</td>
</tr>
<tr>
<td>Glycemia ≥10 or DM (4,092 pts, 61.5%)</td>
<td>1,205 (29.4)</td>
<td>1.06 (0.98–1.14)</td>
<td>0.136</td>
<td>401 (9.0)</td>
</tr>
<tr>
<td>Hypertension (4,742 pts, 72.3%)</td>
<td>1,297 (27.4)</td>
<td>0.80 (0.72–0.88)</td>
<td>-0.0001</td>
<td>396 (8.4)</td>
</tr>
<tr>
<td>Low HDL-C (2,412 pts, 36.3%)</td>
<td>710 (29.4)</td>
<td>1.08 (0.99–1.19)</td>
<td>0.097</td>
<td>254 (10.5)</td>
</tr>
<tr>
<td>High triglycerides (2,298 pts, 34.6%)</td>
<td>612 (26.6)</td>
<td>0.96 (0.87–1.06)</td>
<td>0.425</td>
<td>193 (8.4)</td>
</tr>
</tbody>
</table>

In some disease states, the imbalance of these proteins leads to tissue destruction, proteolysis, and synthesis of cytokines and inflammation. Two intermediate-sized studies indicated that TIMP-1 predicts prognosis. We investigated TIMP-1 levels to predict all-cause mortality in the AGES-Reykjavik Study.

Methods: Participants in this study represent 5721 of the 5764 community-dwelling men and women characterized by the AGES-Reykjavik Study and followed by the Icelandic Heart Association since 1967. We measured TIMP-1 using an ELISA assay in citrate plasma drawn in 2002-2006 in participants and related results to all cause mortality.

Results: At the time of blood sampling, the mean age was 77 years (range 66-98); 58% were female; hypertension was treated in 64%, diabetes was present in 13%, and 12% were active smokers. Of the 5721 participants in the study, 39% died with a median follow-up of 8 years.

Kaplan Meier survival analysis showed higher quartiles of TIMP-1 were associated with all-cause mortality (Fig 1). Both Kaplan Meier and Cox analyses suggested a potential threshold effect where mortality risk elevates after TIMP-1 levels surpass a threshold. Cox multivariable regression analysis adjusted for the cardiovascular risk factors: age, gender, hypertension, smoking status and diabetes found TIMP-1 had the second highest Wald Chi-square score (after age) in the adjusted model.
Conclusions: Troponin I measured by an on-assay was detectable in almost all subjects. This is the first population-based prospective study with long-term follow-up showing that even modestly increased concentrations of us troponin I are strongly associated with incident CHD independently of a variety of traditional risk factors.

1136 | BEDSIDE
High-sensitivity cardiac troponin i predicts long-term cardiovascular outcomes in the west of Scotland coronary prevention study
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Background: The West of Scotland Coronary Prevention Study compared pravastatin versus placebo in middle-aged men without a history of myocardial infarction. We evaluated the association between baseline troponin concentration and cardiovascular events over 15 years follow-up, and the impact of statin therapy on troponin at 1 year.

Methods: Plasma troponin concentration was measured with a high-sensitivity assay (Abbott Diagnostics) at baseline and 1 year following randomisation to 40 mg of pravastatin or placebo in 3,278 participants. Hospitalization for myocardial infarction or death from coronary heart disease was recorded with a median follow up of 15 years.

Results: Troponin concentration at baseline was an independent predictor of myocardial infarction or death from coronary heart disease (p ≤ 0.001, Figure). Compared to the first quartile (< 3.1 ng/L), patients in the top quartile (≥ 5.2 ng/L) were at highest risk after adjustment for other risk factors (Hazard Ratio 1.52, 95% CI 1.05 to 2.19, p = 0.017). Troponin concentration at 1 year was reduced in patients on pravastatin (-11.4%, 95% CI 7.4% to -17.2%), but increased in those on placebo (10.5%, 95% CI 5.1% to 16.2%; p < 0.001 between groups).

Conclusion: Cardiac troponin concentration is an independent predictor for cardiovascular events and is reduced by statin therapy. This biomarker has major potential for cardiovascular risk stratification and for use in clinical efficacy or safety trials.

1137 | BEDSIDE
The soluble interleukin 6 receptor and its natural antagonist, sgp130 and the risk of myocardial infarction
I. Moreno, Z. Golabkesh, H. Kaliberg, K. Learder, U. De Faire, B. Gigante. Karolinska Institute, Institute of Environmental Medicine (IMM), Stockholm, Sweden

Aim: To investigate the association of soluble Interleukin 6 receptor (sIL6R) levels with the risk of myocardial infarction (MI) in a large population base case-control study; the Stockholm Heart Epidemiology Program (SHEEP) and to explore whether circulating levels of the soluble gp130 (sgp130), a natural antagonist of the sIL6R, might modify this association.

Methods: 1213 non-fatal MI and 1561 age, sex and residential matched controls from the SHEEP study were investigated. sIL6R (ng/mL) concentrations were measured in available serum samples from 682 cases and 1103 controls. Sgp130 (ng/mL) concentrations were measured in participants exposed to low sIL6R (value < 25th, Q1) and high sIL6R (Q4) (< 5.6) levels compared to controls exposed to low sIL6R (value < 25th, Q1) (n = 424) and to high sIL6R (value > 75th, Q4) (n = 478) levels. MI risk was calculated by unconditional logistic regression models and expressed as odds ratio (OR) with 95% confidence intervals (CI). Risk estimates were adjusted for the matching variables (crude) and for hypertension, diabetes, hypercholesterolemia, body mass index, smoking and non-steroid anti-inflammatory drugs (adjusted model).

Results: sIL6R median and interquartile ranges (IQR) values were higher in cases 43 (32-65) than in controls 41 (32-54), p = 0.0016. High (> 75th = 54.5) sIL6R levels were associated with an increased risk of MI, with an OR of 1.6 (95% CI 1.3-2.0) (crude model) and an OR of 1.4 (95% CI 1.1 -1.8) at adjusted analysis, as compared to sIL6R < 75th. Median (IQR) sgp130 levels did not differ between individuals exposed to low (Q1) and high (Q4) sIL6R (p = 0.83). Compared to low sIL6R (Q1), exposure to Q4 sIL6R increased the MI risk [OR 1.4 (95% CI, 1.0–1.9)] at the crude and at the adjusted analysis [1.2 (95% CI, 0.9–1.7)]. Inclusion of sgp130 in the crude model did not modify this association OR to

Conclusion: Compared to the first quarter (cases 43 (32–65) than in controls 41 (32–54), p = 0.0016. High sIL6R levels were associated with an increased risk of MI. In the presence of high serum sIL6R levels, circulating sgp130 levels seem to modify this association.

1138 | BEDSIDE
Relationship of major cardiovascular events and 18 non- lipid biomarkers in patients with stable coronary disease and metabolic syndrome: a subanalysis of the treating to new targets trial
P.C. Deedwania1, B. Arsenaault2, W. Bao3, N.K. Wenger4, P. Barter5, S.M. Grundy6 on behalf of the Treating to New Targets investigators. 1University of California San Francisco, School of Medicine, Fresno, United States of America; 2Centre de Recherche de l’Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Quebec, Canada; 3Pfizer Inc, New York, United States of America; 4Emory University School of Medicine, Atlanta, United States of America; 5Centre for Vascular Research, University of New South Wales, Sydney, Australia; 6University of Texas Southwestern Medical Center, Dallas, United States of America

Purpose: Non-lipid biomarkers have attracted much interest due to their potential use in predicting adverse cardiovascular (CV) outcomes and identifying individuals at high CV risk. New risk predictors may be particularly useful in patients with a metabolic syndrome (MetS). In the Treating to New Targets (TNT) trial, 10,001 coronary patients were randomized to atorvastatin (ATV) 10 or 80 mg and followed for a median of 4.9 years. In the 5584 MetS patients, relative risk of major CV events (MCVE) was reduced by 29% with ATV 80 vs 10 mg (P = 0.0001). This subanalysis evaluated the predictive value of biomarkers on MCVE risk in statin-treated coronary patients with MetS.

Methods: Biomarkers were measured after an 8-week run-in period on ATV 10 mg (baseline) and after 1-year treatment with ATV 10 or 80 mg. The predictive value of LDL-C, HDL-C, triglycerides and 18 non-lipid biomarkers on risk of MCVE (cardiac death, myocardial infarction, stroke or resuscitated cardiac arrest) was evaluated by Cox proportional hazards model adjusted for age, sex and treatment. Hazard ratios were for each doubling of biomarker concentration.

Results: In 612 MetS patients included in the analysis, baseline levels of triglycerides, HDL-C, Lp(a), NT-proBNP, neopterin and sRAGE were highly predictive of future MCVE (Figure). After 1 year of treatment, only neopterin and NT-proBNP remained predictive of MCVE. Changes in LDL-C, triglyceride, hsCRP, insulin, Lp-PLA2, NT-proBNP, sICAM-1 and sVCAM-1 levels at Year 1 were significantly different between treatment groups.

Conclusions: In statin-treated coronary patients with MetS, baseline levels of triglycerides and HDL-C were the lipids predictive of MCVE; of the 18 non-lipid biomarkers assessed, Lp(a), NT-proBNP, neopterin and sRAGE were associated with future CV events.

1139 | BEDSIDE
Plasma chemerin is a strong and independent predictor of cardiovascular event risk
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Purpose: Associations of the adipokine chemerin with the metabolic syndrome (MetS) and with chronic kidney disease (CKD), two important indicators of increased cardiovascular disease risk, have been reported. In our present study, we aimed to evaluate the relationship of plasma chemerin levels to the relative risk of major cardiovascular events (MCVE) in patients with MetS.

Methods: Plasma chemerin levels were measured in 612 patients (47.5% female, mean age 68.8 years) with MetS, defined as having hypertension, dyslipidemia, and diabetes according to the guidelines of the American Heart Association/National Heart, Lung, and Blood Institute. The primary endpoint was a composite of cardiac death, myocardial infarction, stroke, or resuscitated cardiac arrest (resuscitated cardiac arrest included in the composite endpoint when it occurred within 24 hours of a previous acute event). The secondary endpoints included the individual components of the primary composite endpoint.

Results: Plasma chemerin levels were strongly associated with the primary endpoint (hazard ratio per 1 SD increase in log chemerin: 2.51, 95% confidence interval 1.61 to 3.91, p < 0.001). The association was independent of traditional cardiovascular risk factors and was consistent across subgroups of patients defined by age, sex, diabetes status, and the presence or absence of CKD.

Conclusions: Plasma chemerin levels were strongly and independently associated with the risk of major cardiovascular events in patients with MetS.
creased cardiovascular event risk, have been described. However, the power of chemerin to predict cardiovascular events has not been investigated so far and is addressed in the present study.

Methods: We measured plasma chemerin in a high-risk cohort of 495 patients undergoing coronary angiography for the evaluation of suspected or established coronary artery disease (CAD) in which cardiovascular events were prospectively recorded over 3.5±1.1 years. Significant baseline CAD was diagnosed in the presence of coronary artery stenoses ≥50.

Results: Baseline plasma chemerin was significantly higher in patients with the outcome, and from the baseline presence of CAD. p=0.015; and 1.69 [1.07-2.67], p=0.024, respectively. With standardized hazard ratios of 1.83 [1.19-2.83], p=0.006; 1.77 [1.12-2.80], p=0.026; 0.91 [0.65-1.28], p=0.05. Levels of TL4R were higher in the CAD group than in the non-CAD group (P <0.01) and were negatively correlated with levels of TL4R-responsive microRNAs (TL4R MFI vs. miR-31: r = -0.47, P <0.01; TL4R MFI vs. miR-16: r = -0.26, P <0.05; TL4R MFI vs. miR-145: r = -0.28, P <0.05). ROC curve analysis showed that a panel of these four circulating miRNAs has substantial diagnostic potential with an AUC of 0.93 (95% CI = 0.87-0.99) for the detection of CAD. Both ARB and ACEI groups showed increased TL4R-responsive miRNAs and diminished levels of TL4R protein (all P <0.01). Changes in miRNAs and TL4R levels were greater in the ARB group than in the ACEI group (P <0.05).

Conclusion: In conclusion, circulating TL4R-responsive miRNA panel may be novel diagnostic and therapeutic biomarker for patients with CAD.

1140 | BENCH
Progression of kidney disease in non-diabetic patients with hypertension: Predictive role of circulating visfatin
C.-Y. Hsu, P.-H. Huang, J.-W. Chen, S.-J. Lin. Taipei Veterans General Hospital, Division of Cardiology, Taipei, Taiwan

Purpose: Declining renal function, estimated by the glomerular filtration rate (GFR), is a significant risk factor for all-cause mortality and primary cardiovascular disease in cardiovascular disease (CVD). Previous evidence showed endothelial dysfunction and systolic blood pressure (SBP) were associated with GFR loss after adjustment for body mass index (BMI) and eGFR, and also after additional adjustment for the presence of significant baseline CAD, the estimated annual rate of GFR decline (ΔGFR/y) was -1.26±2.76 mL/min/1.73 m² per year during the follow-up period (103±30 months). The ΔGFR/y was correlated with the visitatin level, baseline GFR, FMD, SBP, and fasting blood glucose (FBG). Multivariate analysis indicated that increased visfatin (r = -0.331, P <0.001), baseline GFR (r = -0.234, P <0.001), BMI (r = -0.163, P <0.05), and FBG (r = -0.160, P <0.05) are independent predictors of ΔGFR/y. When we divided the patients into 4 groups according to the visfatin levels, there were significant differences in ΔGFR/y among these groups (P =<0.001). There was no statistically significant difference in clinical characteristics between exposed and control subjects. No significant relationships were found between cf-DNA and age, gender, smoking and other clinical parameters. Cf-DNA levels were significantly higher in interventional cardiologists compared to the non-exposed group (44.2±3.38 vs. 30.8±1.18 ng/mL, P =0.04).

1141 | SPOTLIGHT
Circulating toll-like receptor 4-responsive microRNA panel is a biomarker for coronary artery disease: results from a randomized study of treatment with renin-angiotensin system blockades
M. Satoh, Y. Takahashi, T. Tabuchi, M. Tamada, K. Takahashi, T. Itoh, Y. Morino, M. Nakamura. Iwate Medical University School of Medicine, Morioka, Japan

Background: The extracellular microRNAs (miRNAs) circulate in the bloodstream and may serve as novel diagnostic and therapeutic biomarkers. The aim of this study was to investigate circulating miRNA expression in patients with coronary artery disease (CAD), and to examine the effects of renin-angiotensin system (RAS) blockades on miRNA levels.

Methods: This study included 41 patients with CAD (mean age, 66.4±13.2; %male, 85%) and 20 subjects without CAD (NON-CAD) (mean age, 61.6±12.5; %male, 85%). Plasma miRNA profiling was analyzed using microarray assay for 1,700 human miRNAs. The candidate miRNAs were verified with real-time PCR. The amount of Toll-like receptor 4 (TLR4) and CD14 on peripheral blood mononuclear cells was measured by FACS. Patients randomized with CAD (n=20) were randomized to 12 months of combined treatment with either telmisartan (ARB) or enalapril (ACEI). Plasma samples and PBMCs were obtained from peripheral blood at baseline and after 12 months.

Results: The microarray assay showed significant differences in 22 miRNAs between the CAD and non-CAD groups (P<0.05). Real-time PCR verified that the 4 TLR4-responsive miRNAs were among the 22 miRNAs that were significantly down-regulated in the CAD group versus the non-CAD group (miR-31: 1.56±0.74 vs. 2.78±0.92, miR-181a: 1.91±1.05 vs. 3.69±2.21, miR-16: 1.78±0.55 vs. 3.51±1.85: miR-145: 1.69±0.29 vs. 2.47±0.90: CAD group vs. non-CAD group, all P<0.05). Levels of TL4R were higher in the CAD group than in the non-CAD group (P <0.01) and were negatively correlated with levels of TL4R-responsive microRNAs (TL4R MFI vs. miR-31: r = -0.47, P <0.01; TL4R MFI vs. miR-16: r = -0.26, P <0.05; TL4R MFI vs. miR-145: r = -0.28, P <0.05). ROC curve analysis showed that a panel of these four circulating miRNAs has substantial diagnostic potential with an AUC of 0.93 (95% CI = 0.87-0.99) for the detection of CAD. Both ARB and ACEI groups showed increased TL4R-responsive miRNAs and diminished levels of TL4R protein (all P <0.01). Changes in miRNAs and TL4R levels were greater in the ARB group than in the ACEI group (P <0.05).

Conclusion: In conclusion, circulating TLR4-responsive miRNA panel may be novel diagnostic and therapeutic biomarker for patients with CAD.

1142 | BENCH
Elevated levels of circulating cell-free DNA in interventional cardiologists occupationally exposed to low levels of ionizing radiation
A. Borghini1, A. Mercuri1, S. Turchi1, E. Piccaluga2, G. Guagliumi2, E. Picano3, M.G. Andreassi1 on behalf of Healthy Cath Lab (HCL) Study Group of the Italian Society of Invasive Cardiology (ISIE). 1 CNR Institute of Clinical Physiology, Pisa, Italy; 2 Cardiology Unit- Hospital Sacco, Milano, Italy; 3 Cardiovascular Department- Ospedale Papa Giovanni XXIII, Bergamo, Italy

Purpose: Circulating cell-free DNA (cfDNA) is a marker of cell death and tissue injury, and has been used as a risk factor for all-cause mortality and chronic radiation exposure on serum cfDNA levels in interventional cardiologists working in high-volume cardiac catheterization laboratory and exposed to chronic doses of ionizing radiation.

Methods: We enrolled 50 interventional cardiologists (26 males; age=48.4±10 years) and 50 age- and gender-matched unexposed controls (27 males; age=47.6±8.3 years). Quant-IT™ dsDNA High-Sensitivity assay was used to measure circulating cfDNA isolated from serum samples.

Results: There was no statically significant difference in clinical characteristics between exposed and control subjects. No significant relationships were found between cf-DNA and age, gender, smoking and other clinical parameters. Cf-DNA levels were significantly higher in interventional cardiologists compared to the non-exposed group (44.2±3.11 vs. 30.6±19.2 ng/mL, P <0.05). The exposed group with>10 years of work showed significantly increased serum concentrations of cf-DNA (49.2±3.38 vs. 30.8±18.1 ng/mL, P=0.04).

Conclusion: Our data showed increased levels of cf-DNA in interventional cardiologists in controls, providing evidence for its potential role of relevant biomarker to monitor the cellular damage induced by exposure to chronic low-dose radiation.
function, LV mass index and presence/extent of LGE. Feature-tracking analysis was applied to LV basal and apical short-axis images to determine peak basal and apical rotation, peak LVT, time to peak LVT, peak LVUT rate and time to peak LVUT rate.

Results: Peak LVT in CA patients was significantly impaired compared to controls (11.3±4.0° vs. 15.0±1.6°; p<0.05), due to an impairment of peak basal rotation (-2.9±2.5° vs. -7.0±0.7°; p<0.001). Conversely, peak LVT in HCM patients was significantly higher compared to control subjects (18.9±6.7° vs. 15.0±1.6°; p<0.05), due to an increase in peak apical rotation (12.9±5.5° vs. 8.3±1.4°; p<0.01). Peak LVUT rate was significantly impaired in CA patients compared to control subjects (-83.4±22.6°/sec vs. -112.2±26.4°/sec; p<0.05), while it was preserved in HCM patients (-107.3±37.2°/sec vs. -112.2±26.4°/sec; p=0.05). Time to peak LVUT rate was significantly prolonged in both CA and HCM patients compared to controls of LV systole vs. 133±23°/sec vs. 113±6°/sec (ANOVA p<0.001). At ROC curve analysis, peak basal rotation >-5.9°; peak LVUT rate ≤13.8° and peak LVUT rate >-81° had the highest sensitivity and specificity for identification of patients with CA (100% and 83%, 75% and 80% and 55% and 95%, respectively), peak apical rotation >-11° and peak LVT >-17° had the highest sensitivity and specificity for identification of patients with HCM (75% and 83% and 65% and 100%, respectively). At multivariate analysis, age (p<0.007), LV ejection fraction (p<0.03) and extent of LGE (p<0.004) were independently related to peak LVT, LV mass index (p<0.015) and extent of LGE (p<0.004) were independently related to peak LVUT rate, while extent of LGE (p<0.001) was the only variable independently related to time to peak LVUT rate.

Conclusions: CA and HCM have specific behavior of LV rotational mechanics. The extent of LGE significantly influences the LV rotational mechanics.

1148 | BEDSIDE
Pericardectomy improves right ventricular echocardiographic mechanics

Background: Complete pericardial resection is the definitive treatment for patients with constrictive pericarditis (CP). Two-dimensional speckle tracking echo (2D-STE) has not routinely been used to assess right ventricular (RV) function in CP patients. The aim of this study was to evaluate RV mechanics using 2D-STE in patients with CP undergoing pericardectomy.

Methods: One hundred and fourteen CP patients (mean age 62 years, 65% male) were included in this study. All echocardiographic images were prospectively analyzed offline using 2D-STE technology. Patients were divided into 3 groups: radiotherapy or previous cardiac surgery (R-CP), complete pericardectomy among the three groups. After adjusting for age, sex, body mass index and RV dysfunction severity did not significantly affect strain improvement post-pericardiectomy among the three groups. Basal rotation (-2.9° vs. -12°) and early phase rather than a specific disease and it presents benign long-term outcome. However, long-term outcome of BP A, especially the cumulative survival of technical limitations. Recently, we reported our initial experience with balloon pulmonary angioplasty (BP A) for 68 inoperable patients with CTEPH. In this report, exercise capacity and hemodynamics were significantly improved. At follow up (average 4.9±1.6 yrs), exercise capacity and hemodynamics at baseline, immediate after BP A and follow up. In addition, autonomic (by DE) cardiac involvement in a significant percentage of SSc patients, often overt systolic or diastolic left ventricular dysfunction on echocardiography. The association between a history of radiotherapy and myocardial fibrosis may suggest a similar pathological substrate of abnormal vascular function, underlying cutaneous and cardiac complications.

Conclusions: CMR can detect patterns of reversible (by T2-weighted) and irreversible (by DE) cardiac involvement in a significant percentage of SSC patients, often overt systolic or diastolic left ventricular dysfunction on echocardiography. The association between a history of radiotherapy and myocardial fibrosis may suggest a similar pathological substrate of abnormal vascular function, underlying cutaneous and cardiac complications.

1150 | BEDSIDE
Clinical and instrumental characterization and the long-term prognosis of Mildly Dilated Cardiomyopathy

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Purpose: To define the clinical and instrumental characterization and the long-term prognosis of Mildly Dilated Cardiomyopathy (MDCM). MDCM is a subgroup of idiopathic dilated cardiomyopathy (IDCM) characterized by slightly dilated left ventricle and presenting systolic dysfunction. The long-term evolution and the diagnostic process are different due to the disease is unknown in the current treatment and clinical management era of IDCM.

Methods: From 1988 to 2008 we enrolled 659 patients with IDCM; MDCM was considered in presence of LVEF <50% and LV end-diastolic volume index (LVEDVI) >86 ml/m² at echocardiographic evaluation.

Results: 252 patients (38%) fulfill the pre-specified criteria for MDCM. At baseline evaluation MDCM patients were less symptomatic than IDCM patients (NYHA III/IV 15% vs 30% respectively, p<0.001) and had a slightly higher LVEF (36±8 vs 30±12%, p<0.001). Interestingly MDCM patients initially improved under optimal therapy, then were stable in mid-term, followed by a progression in the long-term approaching the condition of other IDCM patients. At 10 years follow up mortality for all causes death was 21% in MDCM and 39% in IDCM (p<0.001); heart failure death/HTx and sudden death/malignant ventricular tachycardia rates were 10% vs 18% (p=0.002) and 12 vs 20% (p=0.005) in MDCM and IDCM patients respectively. MDCM with baseline LVEF <35%, compared to the other MDCM patients, presented lower survival rates (p<0.001) but similar rates of long-term sudden death and malignant ventricular arrhythmias (p=0.6).

Conclusions: MDCM identified a consistent subgroup of patients with CTEPH discovered in an early phase rather than a specific disease and it presents benign long-term outcome. Initially it is characterized by a less adverse evolution, however it presents a long time progression approaching the other IDCM. Baseline LVEF cut-off of 35% is not helpful in predicting the risk of major arrhythmic events in MDCM.
eraged 16.0 months), none of them experienced restenosis or recurrence of pulmonary hypertension even after the discontinuation of pulmonary hypertension-specific drugs. Exercise capacity at follow up were unchanged, whereas hemodynamics were additionally improved compared to that at immediate after BPA. The long term favorable effect of BPA on hemodynamics resulted in good survival rate of our patients treated with BPA. Cumulative survival rate at 1-, 2-, 3- and 5-year was 96, 95 and 90%, respectively.

Outcome of BPA

<table>
<thead>
<tr>
<th>Pre BPA</th>
<th>Immediate after BPA</th>
<th>Follow up (N=89)</th>
</tr>
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<tr>
<td>WHO FC</td>
<td>3.0±0.36</td>
<td>2.0±0.37</td>
</tr>
<tr>
<td>m60W (m)</td>
<td>265.0±12.9</td>
<td>360.0±17.4</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>42.1±1.06</td>
<td>26.0±4.8</td>
</tr>
<tr>
<td>PVR (dyne.s.cm⁻⁵)</td>
<td>694.7±520.3</td>
<td>362.5±117.2</td>
</tr>
</tbody>
</table>

(Conclusion) Refined BPA could improve exercise capacity and hemodynamics of inoperable patients with CTEPH. Additional improvement of hemodynamics after long term follow up resulted in good survival rate of them treated with BPA. Refined BPA would be a better alternative to medicinal treatment for inoperable patients with CTEPH.

1152 | BEDSIDE
Percutaneous transluminal pulmonary angioplasty improves right ventricular function in patients with inoperable chronic thromboembolic pulmonary hypertension

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Purpose: Recent studies have demonstrated that percutaneous transluminal pulmonary angioplasty (PTPA) improves pulmonary hemodynamics in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH). In this study, we examined whether PTPA also improves right ventricular (RV) dysfunction in these patients.

Methods: We performed a total of 232 PTPA procedures (median 4.5 procedures per patient) for 48 consecutive patients with inoperable CTEPH (median age 64 yrs, 77.1% female). Before PTPA, we treated all patients with optimal medical treatment and performed right heart catheterization before and after PTPA. RV function was evaluated by tricuspid annular plane systolic excursion (TAPSE) on echocardiogram (n=18, 37.5%) and RV ejection fraction (RVEF) on cardiac magnetic resonance imaging (n=9, 19%) before and after PTPA.

Results: No patient died during the PTPA procedure or during a median follow-up period of 8.5 months. Comparisons before and after PTPA showed significant hemodynamic improvements for mean pulmonary artery pressure (41.1±3.3 to 25.7±5.5mmHg, P<0.001), cardiac index (2.2±0.5 to 2.7±0.6 L/min/m², P<0.001) and RVEF (73.8±3.45 to 283.9±97.97 dynes/sec cm, P<0.0001). Furthermore, RV function was also significantly improved for both TAPSE (18.3±3.3 to 21.6±2.8mm, P<0.004) and RVEF (39.6±8.8 to 52.1±7.3%, P<0.001) (figure).

Conclusions: PTPA improves not only pulmonary hemodynamics but also RV function in patients with inoperable CTEPH.

1153 | BEDSIDE
Either balloon pulmonary angioplasty or surgical pulmonary endarterectomy can cover most patients with chronic thromboembolic pulmonary hypertension as treatment option

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Aims: Pulmonary endarterectomy (PEA) is the standard therapy for chronic thromboembolic pulmonary hypertension (CTEPH); however, up to 40% of patients are non-operative. Recently, the efficacy of balloon pulmonary angioplasty (BPA) for non-operative patients has been reported, as the procedure becomes more refined. We evaluated the efficacy and safety of BPA for non-operative CTEPH patients as well as of surgical PEA in operable CTEPH.

Methods: Consecutive 60 CTEPH patients were reviewed retrospectively. Twenty-five operable patients underwent PEA (57±1.36 years old, San-Diego type I: 11, II: 3, III: 11, IV: 0), and 32 non-operable patients underwent BPA (67±1.15 years old, San-Diego type I: 0, II: 4, III: 20, IV: 8). BPA was repeated in 1 to 6 sessions to every patient depending on their severity. Three patients did not consent with any invasive procedure because of advanced age.

Results: Although proportion of San Diego classification was different between PEA and BPA group, both PEA and BPA significantly improved hemodynamics and symptoms similarly, such as a significant increase in cardiac output (CO) and decrease in mPAP and pulmonary vascular resistance (PVR) (Table). Reperfusion pulmonary injury occurred in 3 patients (12.0%) after PEA, and in 27 sessions (28.4%) after BPA with 3 sessions required emergent intubation. The mortality rates of PEA and BPA were 8.0% and 3.1%, respectively (P=NS).

Table 1

<table>
<thead>
<tr>
<th>BPA (n=32)</th>
<th>Baseline</th>
<th>Post procedure</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>m60W (m)</td>
<td>3.3±0.6</td>
<td>0.43</td>
<td>5.6±2.8</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>38.9±7.1</td>
<td>21.1±5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PVR (dyne.s/cm²)</td>
<td>761±333</td>
<td>285±137</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHO FC (I/II/III/IV) (0/4/20/8) (12/16/3/0)</td>
<td>(5/0/4/1)</td>
<td>(2/6/7/0)</td>
<td>(1/0/0/0)</td>
</tr>
<tr>
<td>PE (n=25)</td>
<td>3.3±1.08</td>
<td>4.4±1.54</td>
<td>0.006</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>43.9±11.0</td>
<td>21.6±6.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PVR (dyne.s/cm²)</td>
<td>772±273</td>
<td>262±123</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHO FC (I/II/III/IV)</td>
<td>(2/3/1/4)</td>
<td>(13/8/2/0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: The efficacy and safety of BPA for non-operative cases were similar to those of PEA for operable cases. Most CTEPH patients can be satisfactorily treated by BPA or PEA.
ute whether a single dose of oral sildenafil can influence the SVI response to exercise in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

**Methods:** Fourteen CTEPH patients and 8 healthy controls underwent cardiac magnetic resonance (CMR) imaging at rest and during incremental supine bicycle exercise to near-maximal exertion with simultaneous invasive hemodynamic monitoring. During real-time exercise and free-breathing, left and right ventricular (LV and RV) volumes were derived from real-time cine imaging and registered with simultaneous invasive measures of mean pulmonary artery pressure (mPAP). Exercise was performed at baseline and then following administration of 50mg oral sildenafil.

**Results:** As illustrated in Figure 1, CTEPH patients had a greater increase in mPAP relative to cardiac output (CO) than controls at baseline (8.6±1.9 vs. 1.5±0.3 mmHg/l/min; P=0.002). In addition, SVI and RV ejection fraction (RVEF) increased during exercise in controls, but not in CTEPH patients (interaction group*workload P<0.0001). Sildenafil decreased the slope of the mPAP/CO relationship both in CTEPH patients (P=0.02) and in controls (P=0.09). However, this was associated with an increased SVI in CTEPH patients (P<0.05), but not in controls. Within the CTEPH cohort, the increase in SVI following sildenafil was greater during near-maximal exercise-intensity than at rest (P=0.02).

**Conclusions:** Sildenafil improves RV function and stroke volume during exercise in patients with CTEPH, but not in healthy subjects.

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**CLINICAL PHENOTYPES AND OUTCOMES IN CARDIOMYOPATHIES**

**1193 | BEDSIDE**

**Structural myocardial substrate is a prerequisite for malignant ventricular arrhythmias and sudden death in carriers of ARVC-causing desmosomal gene mutations**

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**Background:** Experimental studies raised the hypothesis that mutations of genes encoding for desmosomal (DS) proteins may “per se” induce electrical ventricular instability and life-threatening arrhythmia independently of development of a structural myocardial substrate. This study assessed whether the occurrence of malignant arrhythmic events among carriers of DS-gene mutations depends on phenotypic expression of arrhythmogenic right ventricular cardiomyopathy (ARVC).

**Methods:** The study population included 123 DS-gene mutation carriers (62 males; median age 29 (15–47) years) with no history of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) at the time of first clinical evaluation. The cumulative probability of experiencing VT/VF or SCD was evaluated prospectively during a long-term follow-up and stratified by presence and severity of the ARVC phenotype. ARVC was classified as “definite” or “borderline” according to the 2010 International Task Force (ITF) criteria and its phenotypic expression graded as mild or severe on the basis of presence of epsilon waves, extent of negative T-wave and severity of RV dilatation/dysfunction.

**Results:** At the time of first clinical evaluation, 69 of 123 (56%) subjects fulfilled the ITF diagnostic criteria for ARVC (genotype + phenotype +), either “definite” (N=51; 41%) or “borderline” (N=18; 15%), while 54 (44%) did not (genotype + phenotype –). During a median follow-up of 7 (5-12) years, 11 subjects had arrhythmic events such as sustained VT (N=9), appropriate ICD shock on VF (N=1) and SCD (N=1). All patients who reached the arrhythmic end-point had a diagnosis of “definite” ARVC, whereas genotype + phenotype – subjects and “borderline” ARVC patients had an eventful long-term outcome (p<0.001). Among patients with “definite” ARVC, a severe phenotype was associated with a significantly higher rate of arrhythmic events than that of a mild phenotype (38% vs 4%; p=0.002).

**Conclusions:** The study results suggest that the development of a structural myocardial substrate is a prerequisite for malignant ventricular arrhythmias and SCD in carriers of ARVC-causing desmosomal gene mutations. These findings have significant implications for clinical monitoring and risk assessment of ARVC genotype + phenotype – subjects.
and the current guidelines.

0.73, \( p=0.1 \). Figure 1 shows the ROC curves for the novel risk prediction model 0.71 (95% CI 0.60–0.81, \( p=0.002 \)) which performed significantly better than the patients (age 49

Results: Current risk stratification models for sudden cardiac death (SCD) in hypertrophic cardiomyopathy (HCM) are suboptimal. The recent HCM Risk-SCD study (O’Mahony et al. Eur Heart J, 2013) proposed a novel risk prediction model to improve decision-making for prophylactic ICD implantation in individual HCM patients. This study is an external and independent validation of this novel risk prediction model.

Methods: The study population consisted of a consecutive cohort of 706 HCM patients without prior SCD event, from 2 tertiary referral centers. Primary endpoint was a composite of SCD and appropriate ICD therapy, identical to the HCM Risk-SCD formula. Receiver operating characteristic (ROC) curves and C-statistics were calculated for the HCM Risk-SCD score, and the 2003 ACC/ESC guidelines and 2011 ACCF/AHA guidelines.

Results: During follow-up (7.7±5.3 years), SCD occurred in 42 (5.9%) of 706 patients (age 49±16 years, 36% female). The C-statistic of the new model was 0.71 (95% CI 0.60–0.81, \( p=0.002 \)) which performed significantly better than the conventional risk factor models based on the 2003 guidelines (C-statistic of 0.63; 95% CI 0.51–0.74, \( p=0.05 \)) and 2011 guidelines (C-statistic of 0.60; 95% CI 0.47–0.73, \( p=0.1 \)). Figure 1 shows the ROC curves for the novel risk prediction model and the current guidelines.

Figure 1

Conclusion: The recently developed HCM Risk-SCD score significantly improves the risk stratification of individual HCM patients, as compared to the existing risk stratification methods.

1196 | BEDSIDE

Independent validation of the novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM Risk-SCD)

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Purpose: Current risk stratification models for sudden cardiac death (SCD) in hypertrophic cardiomyopathy (HCM) are suboptimal. The recent HCM Risk-SCD study (O’Mahony et al. Eur Heart J, 2013) proposed a novel risk prediction model to improve decision-making for prophylactic ICD implantation in individual HCM patients. This study is an external and independent validation of this novel risk prediction model.

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Figure 1

Conclusion: The recently developed HCM Risk-SCD score significantly improves the risk stratification of individual HCM patients, as compared to the existing risk stratification methods.

1197 | BEDSIDE

Prevalence and age distribution of hypertrophic cardiomyopathy phenocopies: data from a single center including both adults and children


Purpose: We evaluated the prevalence and age distribution of hypertrophic cardiomyopathy (HCM) phenocopies in a large population including both children and adults.

Methods: Aetiological diagnosis was made in 776 HCM phenotype patients (0–94 yrs) on the basis of clinical/instrumental features, molecular biology, enzymatic dosages, biopsy, magnetic resonance imaging and 99mTc-DPD scintigraphy. The distribution of aetiologies according to age decades is shown in the table and was strongly age-dependent.

1206 | BEDSIDE

Self-expandable versus balloon-expandable devices in patients with mixed aortic valve stenosis undergoing transcatheter aortic valve implantation: results from a single-center registry

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Objectives: The aim of this study was to compare outcomes in patients with mixed aortic stenosis (MAS), undergoing transcatheter aortic valve implantation (TAVI) via a transfemoral (TF) approach with the Medtronic CoreValve (MCV) versus Edwards-SAPIEN or SAPIEN XT Valve (ESV).

Background: Prevalence of MAS in patients undergoing TAVI is unclear. Due to the particular pathophysiology of this condition, these patients could represent a high-risk group with regards to device malpositioning, post-procedural aortic regurgitation and other complications. To date no study has evaluated the performance of the commercially available MCV and ESV in this particular subgroup of patients.

Methods: From November 2007 to September 2013 all patients with a documented baseline MAS condition that underwent transfemoral (TF) TAVI either with MCV or ESV, were included in this analysis. MAS patients were defined by the presence of at least moderate aortic stenosis (AS) associated with moderate or severe aortic regurgitation (AR). Outcomes were assessed according to valvular academic research consortium (VARC-2) criteria at 30 days, 1 and 2 years.

Results: Among 472 patients in whom a baseline echocardiographic data were available, 295 (62.4%) had a pure aortic stenosis (PAS) while 177 had MAS (37.6%). Of 177 MAS patients, 59 (33.3%) were treated with MCV and 83 (46.8%) with ESV through a TF approach. At 30 days there were no differences in all-cause mortality (5.2% vs. 2.4%; \( p=0.391 \)), cardiovascular mortality (3.4% vs. 2.4%; \( p=0.724 \)), device success (58.6% vs. 67.5%; \( p=0.282 \)) or early safety endpoint (34.5% vs. 25.3%; \( p=0.237 \)). However, a greater incidence of valve embolization (7.5% vs. 0%; \( p=0.013 \)), need for a second valve (9.4% vs. 0%; \( p=0.005 \)), permanent pacemaker implantation (28.8% vs. 9.8%; \( p=0.010 \)) and moderate to severe peri-prosthetic AR (PP AR; 12.1% vs. 0%; \( p=0.001 \)) was found in the MCV group.

Finally, at 1 year there were no differences in all-cause and cardiovascular mortal- ity (15.5% vs. 12.2%; \( p=0.572 \), and 12.1% vs. 4.9%; \( p=0.119 \)). Conversely, at 2 years, a greater all-cause (29.3% vs. 14.6%; \( p=0.035 \)) and cardiovascular mortality (21.1% vs. 4.9%; \( p=0.001 \)) was found in the MCV group.

Conclusions: MCV was associated with a greater incidence of moderate-to-severe PP AR and other intra- and peri-procedural complications in MAS patients that underwent TAVI. No significant differences were found in mortality at 30 days

Abstract 1197 – Table 1. Distribution of the different aetiologies according to age decades

Phenocopies

<table>
<thead>
<tr>
<th>Age group</th>
<th>N=69</th>
<th>N=38</th>
<th>N=52</th>
<th>N=75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic HCM (presumably sarcomeric)</td>
<td>44 (64)</td>
<td>34 (89)</td>
<td>46 (88)</td>
<td>69 (82)</td>
</tr>
<tr>
<td>Wild type TTR amyloidosis</td>
<td>0</td>
<td>0</td>
<td>2 (4)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>AL amyloidosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant TTR amyloidosis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Malignant hyperthermia</td>
<td>8 (12)</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td>11 (1)</td>
</tr>
<tr>
<td>Anderson-Fabry disease</td>
<td>0</td>
<td>0</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Neuromuscular diseases</td>
<td>5 (7)</td>
<td>2 (5)</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Mitochondrial diseases</td>
<td>5 (7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Glycogen storage diseases</td>
<td>4 (6)</td>
<td>0</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Newborns of diabetic mothers</td>
<td>3 (4)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
and 1 year between the 2 valve groups. However a greater all-cause and cardiovascular mortality was found in patients treated with the MCV at 2 year follow-up.

1207 | SPOTLIGHT
Effective orifice area and hemodynamic performance of the 14Fr transcatheter colibri heart valve compared with the SAPIEN and CoreValve TAVI

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Background: Transcatheter heart valve implantation has emerged as a technology to replace the aortic valve of patient with high surgical risk. Current available technology approved includes the Sapien and the Corevalve that have shown better hemodynamics than the surgical valves. In November 2012, the first in human series of the Colibri heart valve were implanted in our center. The Colibri Heart Valve is the first pre-package, pre-mounted, low profile, dry valve that is ready to be used from its 14F introducer to the patient.

We sought to compare the Effective Orifice Area (EOA) and hemodynamic performance of these three devices within the first 30 days following implantation.

Methods: Doppler hemodynamics were performed before and after implantation of the Colibri Heart Valve (CHV) in five consecutive patients. Gradient across the valve was assessed using continuous Doppler. EOA was calculated using the left ventricular outflow tract (LVOT) area multiplied by the ratio of the time velocity integral (TVI) of the LVOT measured with pulse Doppler and the TVI across the Colibri Heart Valve recorded with continuous Doppler. These findings were compared using t-test and ANOVA with published data for the Sapien 23mm valve (n16) and the 26mm Corevalve (n40).

Results: The mean gradient of the 23mm internal diameter CHV was 8.4 ± 3.4mmHg versus 11.9 ± 4.2 of the 23mm Edward’s Sapien and 8.4 ± 3.8 for the 26mm CoreValve. The EOA of the CHV was 2.18cm² ± 0.17 versus 1.47cm² ± 0.14 for the 23mm Sapien (p=0.0001) and 1.78cm² ± 0.4 for the 26mm Corevalve (p=0.0169).

Conclusion: Colibri Heart Valve showed lower gradients and statistically significantly higher EOA than the 23mm Sapien and the 26mm Corevalve when measured within the first 30 days post implantation.

1208 | BEDSIDE
Hemodynamic assessment of percutaneous versus surgical bioprostheses for aortic stenosis during exercise: a pilot study

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Background: Poor hemodynamic performance as assessed by transprosthetic gradient (TG) after aortic bioprosthesis implantation is associated with less symptomatic improvement and worse prognosis. This effect is magnified in smaller bioprostheses. Transcatheter aortic valve implantation (TAVI) has been associated with lower TG when compared to surgical aortic valve replacement (SAVR) in previous studies. However, no data are available on the hemodynamic response to exercise in this population.

Aim: To assess the hemodynamic performance of TAVI versus SAVR in small sized valves at rest and exercise

Methods: Twenty patients (P) were prospectively assessed, consisting of 10 P submitted to TAVI with the Corevalve prostheses (23 & 26) and 10 age-matched SAVR controls with similar valve dimensions, who had been submitted to valve implantation within a similar interval. A symptom-limited treadmill exercise protocol (EP) modified for frail/elderly patients was used. Echocardiographical evaluation was performed at rest and peak exercise.

Results: No significant differences between groups were found on patient age (TAVI 81.7 ± 6.6y vs SAVR 80.2 ± 3.37 y), BMI (25.0 ±0.9 vs 27.8 ±1.15, all p=NS) or time since implantation (17.2 ±3.6 vs 14.7 ±5.3 months, p=NS). The logistic Euroscore was higher in TAVI patients (15.2% vs 8.7%; p=0.013).

SAVR patients were more likely to be under betablocker therapy (20% vs 70%, p=0.025), with no other differences in medication. Max heart rate during EP was 107 ±10.9 vs 121 ±10.4 and exercise duration was 7.21 ± 1.8 vs 14.0 ± 4.7 minutes (p=0.002). No differences were found on left ventricular (LV) ejection fraction (EF) (LVEF <50%; 30% vs 20%) or LV dimensions (LV end-diastolic diameter (d) 50.8 ±2.3 vs 50.5 ±2.6, LV end-systolic d 29.1 ±1.9 vs 31.8 ±2.3, p=NS). Resting TG was significantly lower in TAVI patients (Max TG 14.3 ±1.79 vs 21.5 ±1.15, p=0.003, mean TG 7.5 ±1.0 vs 12.5 ±0.8, p=0.0019). TG at peak exercise was also significantly lower in TAVI patients (Max TG 23.3 ±3.1 vs 38.7 ±3.6, p=0.004; mean TG 11.7 ±2.1 vs 21.1 ±2.3, p=0.01). Systolic pulmonary artery pressure, transmural wave velocities and peak LVEF were similar. After multivariate analysis of baseline clinical and echocardiographical variables, TAVI was the only independent predictor of lower max TG at rest and at peak exercise (p=0.032, p=0.023).

Conclusion: Patients submitted to TAVI have a better transprosthetic hemodynamic profile at rest and during exercise than SAVR. TAVI may be a more suitable option in AVR in patients when a small diameter bioprosthetic valve is implanted.

1209 | BEDSIDE
Impact of mitral ring remodeling after mitraclip procedure in the reduction of functional mitral regurgitation


The Mitraclip (MC) procedure appears to reduce mitral ring diameters in patients with functional etiology but it is unclear whether this reduction has relation with the severity of MR postprocedure.

The objective was to investigate if the remodeling of the mitral ring with the MC procedure has some impact in the reduction of MR in patients with functional etiology.

Methods: From October 2012 to January 2014 all patients with functional MR who were treated with a MC in our centre were included in the study. A transthoracic and transesophageal (TEE) 2D an3D echocardiogram was performed immediately before and after placement of the device (EQ3 equipment, Qlab software,Phillips). The changes in mitral ring diameters measured by means of 3DTEE (intercomisural (IC) and anteroposterior (AP)) were correlated with the severity in MR evaluated by the effective regurgitant orifice (ERO).

Results: 18 consecutive patients with functional MR were included (mean age 61±16; 72%males; 66% NYHA functional class III-IV; FEVI 28%±12; pulmonary artery systolic pressure 48±10 mmHg). Immediately post procedure the ERO decreased from 0.49±0.06 to 0.23±0.10cm², p<0.0005. A significant reduction was observed in the AP-diameter of the mitral annulus (29±5 vs 26±5mm, p<0.0005) without changes in IC-diameter (42±4 vs 42±4mm,p=0.76). A significant correlation was observed between the reduction in AP-diameter and the reduction in ERO immediately postprocedure (r=0.55, p=0.017, Fig. 1).

Conclusion: The Mitraclip procedure causes an immediate reduction in AP-diameter of the mitral annulus in patients with functional MR. This remodeling is significantly associated to reduction in MR, evaluated by ERO.
1210 | BEDSIDE
Computed Tomography for the assessment of mitral valve in patients undergoing transcatheter aortic valve

Introduction: Indication of percutaneous aortic valve implantation (TAVI) when simultaneous presence of moderate-to-severe mitral regurgitation (MR) occurs is object of debate. Abbeal multidetector computed tomography (MDCT) is routinely performed to TAVI candidates in many centers, the potential usefulness of this tool to decide which patients with dual valvulopathy may benefit from isolated TAVI is unknown.

Methods: We analysed 94 patients treated with transfemoral self-expandable aortic prosthesis according to the baseline degree of their MR. All clinical and procedural variables were prospectively recorded. An off-line analysis of echocardiographic and MDCT images, including annulus and leaflets semi-quantitative analysis of calcification, was performed in order to determine predictors of MR improvement.

Results: Mean age was 81 ± 7 years, and median STS-score 5.1 [3.8-7.6]%.

- Patients with moderate-to-severe MR (n=42, 44.6%) presented worse left ventricular ejection fraction (55% vs 63%, p=0.006), and higher systolic pressure of pulmonary artery (51 vs 39 mmHg, p=0.001). In 22 pts (52.4%) MR degree improved to mild or none. MDCT independent predictors of MR improvement were: absence of leaflets calcification in 76.5% vs 23.1%, OR=1.92 [95%CI: 0.03-0.79], p=0.026, and mitral annulus size (34.7 ± 3.5 mm vs. 39 ± 3.8 mm), OR=2.61 [95%CI: 0.01-40], p=0.003, with 35.90 mm as the cut-off value in ROC analysis which better predicted MR improvement. Other predictors of MR improvement were: Baseline NYHA functional class <2; absence of calcification of mitro-aortic junction; absence of left bundle branch block; and baseline aortic regurgitation ≥3 as assessed by echo.

Conclusions: More than half of the patients who suffered from simultaneous moderate/severe MR and underwent TAVI had a significant reduction in the degree of MR. MDCT analysis of the mitral anatomy determined that MR improvement was not influenced by mitral annulus calcification but it was inversely related to the diameter of mitral annulus and the degree of calcification of mitral leaflets and mitro-aortic junction.

1211 | BEDSIDE
Surgical cutdown versus percutaneous access in transfemoral transcatheter aortic valve implantation: insights from the brazilian TAVI registry
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Background: Choosing the best strategy for vascular access in patients undergoing transfemoral aortic valve implantation (TAVI) is a crucial step for performing the procedure. Femoral access for TAVI is achieved by surgical cutdown and closure or percutaneous puncture and hemostasis with closing devices. Currently, little is known about the impact of the two access approaches on clinical outcomes after transfemoral TAVI.

Methods: The Brazilian registry is a national study that prospectively and retrospectively enrols patients treated with TAVI. Patients undergoing transfemoral TAVI were divided into two groups and compared according to the vascular access approach (percutaneous vs surgical). The choice of technique was left to the discretion of the operator and local heart teams. All-cause mortality, vascular complications, and life-threatening bleeding were analysed one year post-TAVI.

Results: Of the 402 patients enrolled, percutaneous access was performed in 182 and surgical in 220. Clinical outcomes at 30 days and 1 year is detailed in the following Table.

<table>
<thead>
<tr>
<th>Percutaneous vs surgical approach</th>
<th>Percutaneous approach</th>
<th>Surgical approach</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=182 pts)</td>
<td>(n=220 pts)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality 30 days</td>
<td>8.8%</td>
<td>8.6%</td>
<td>0.9</td>
</tr>
<tr>
<td>All-cause mortality 1 year</td>
<td>25.3%</td>
<td>22.7%</td>
<td>0.7</td>
</tr>
<tr>
<td>Major vascular events</td>
<td>8.8%</td>
<td>8.2%</td>
<td>0.8</td>
</tr>
<tr>
<td>Life-threatening bleeding</td>
<td>9.3%</td>
<td>8.2%</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Conclusion: In transfemoral TAVI, the vascular access strategy (either percutaneous or surgical) is not a major determinant of clinical outcomes one year after the procedure.

1233 | BEDSIDE
Prevalence of risk factors at presentation and early mortality in patients 80 years or older with ST-segment elevation myocardial infarction
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Purpose: Elderly patients with ST-segment elevation myocardial infarction (STEMI) are at high risk of complications and early mortality; still they are underrepresented in clinical trials and observational studies. We aimed to study risk profiles at presentation and early mortality in older (≥80 years) vs. younger (<80 years) STEMI-patients.

Methods: Prospective cohort study. The study population comprised 4092 consecutive STEMI patients admitted to our university hospital during 2006 to 2010. Baseline characteristics at admission were recorded as well as in-hospital mortality. Explanatory strategy was used in the analyses.

Results: Patients ≥80 years (n=536) were more likely to be female, have prior myocardial infarction, angina and stroke, but less likely to be current smokers. The crude in-hospital mortality rate was 16.2% in patients ≥80 years and 3.5% in those <80 years (crude odds ratio 5.41, 95% confidence interval, 4.07-7.3). The adjusted odds ratio for mortality for patients ≥80 vs. <80 years increased with increasing levels of serum creatinine and total cholesterol (Figure). In patients with low levels of serum creatinine and total cholesterol, the odds ratio was 3.01 (95% confidence interval, 1.86-4.93; p=0.0001); increasing to 11.72 (95% confidence interval 5.26-26.3; p=0.001) in patients with high levels of both risk factors.

Conclusion: High levels of serum cholesterol and creatinine were important risk factors for early mortality in elderly patients with STEMI. Depending on the levels of cholesterol and creatinine, in-hospital mortality in patients ≥80 years varied from a three-fold to an almost twelve-fold risk compared to younger patients.

1234 | BEDSIDE
Mental status at presentation as a predictor of outcome in acute coronary syndrome among elderly patients
F. Beygi1, L. Bobolli1, J. Wain-Hobson1, V. Roule1, R. Sablat1, T. Lognme1, J.P. Collet2, G. Montalescot2, P. Milliez1, 1University Hospital of Caen, Department of Cardiology, Caen, France; 2AP-HP - Hospital Pitié-Salpêtrière, Paris, France

Purpose: To assess the impact of mental status alteration (MSA) at presentation for acute coronary syndrome (ACS) on cardiovascular events among elderly.

Methods: After exclusion of patients with unstable conditions, neurological disorders or language deficiency, we assessed MSA defined by an abnormal confusion assessment test or Mini Mental Status Evaluation (MMSE) score, ≥8 in patients <75 years, and ≥5 in patients ≥75 years of age. The adjudicated cox model identified MSA and troponin rise.

Results: MSA was identified in 49 (49%) patients. Patients with MSA were older (84.5 vs 81.5%, p=0.006), had lower body index mass (25.5 vs 27.4, p=0.02), lower education level (primary only in 89 vs 67%, p=0.01), higher rates of coronary artery surgery (12 vs 2%, p=0.04) and higher rates of Killip Class ≥2 (47 vs 35%, p=0.03). The invasive management and medical therapy were similar between patients with or without MSA.

Rates of in-hospital and 3 months mortality were higher in MSA patients (14.3 vs 2%, p=0.02 and 20.4 vs 2%, p=0.003). Rates of any or cardiovascular hospitalization were high and similar between the groups (32.6 vs 27% and 14.3 vs 11.5%). The adjusted cox model identified MSA and MMSE as independent predictors of 3-month mortality (HR 13.4, 95%CI 1.7-105 and HR 0.86, 95%CI 0.8-0.9 respectively).

Conclusions: MSA is detected in almost half of patients ≥75 years old presenting with ACS using simple clinical tests. Despite similar management the rates of in-hospital and 3 months mortality are dramatically increased in such patients. Studies are needed to assess the mechanisms of the disease and the impact of specific management among such high risk patients.
**1235 | BEDSIDE**

Age-dependent improvements in survival after hospitalisation with acute myocardial infarction (AMI)

O. Albas1, V. Allan2, J. Mclenachan2, R. Feltbower1, C. Gale1, 1University of Leeds, Leeds, United Kingdom; 2Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

**Purpose:** Our aim was to investigate age-dependent improvements in survival after hospitalisation with Acute Myocardial Infarction (AMI).

**Methods:** A total of 583,466 patients with AMI admitted to 247 hospitals between January 1, 2003 and December 31, 2010. Six month relative survival (RS) was calculated using an age, sex and biennial year matched population from the Office for National Statistics. Risk adjusted mortality rates (RMAr) were estimated using shared frailty regression. Evidence-based medications were computed as five-drug treatment with aspirin, clopidogrel, beta-blockers, statin and ACE inhibitors.

**Results:** Older patients compared with the younger patients presented more frequently with co-morbid conditions, including Chronic Heart Failure (11.1% vs 1.6%), Chronic Renal Failure (7.8% vs 1.7%) and previous AMI (30.8% vs 15.8%). Older patients were less likely to be admitted to a Coronary Care Unit (39.1% vs 64.0%), be under the care of a Consultant Cardiologist (30.1% vs 51.1%) and less frequently received Evidence-Based Medications after hospital discharge (73.7% vs 85.5%). For STEMI, there was an increase in RS for patients aged 65 to 80 ys (84.8% vs 89.2%) and those over 80 ys (68.0% vs 71.8%), but not for patients aged 18 to 65 ys (96.4% vs 96.9%). For NSTEMI patients aged 18 to 65 ys RS was higher, but stable (95.5% vs 96.8%) and improved for patients aged 65 to 80 ys (83.2% vs 88.5%) and patients aged ≥ 80 ys (69.3% vs 76.5%). Likewise, RMAr improved for patients aged ≥65 ys, were stable and higher for patients <65 ys.

**Conclusions:** There were significant improvements in survival after hospitalisation with AMI in the older but not younger patients. The scope for further reductions in mortality is likely to be much greater for older than younger patients with AMI.

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**1237 | BEDSIDE**

**Mortality and neurological outcome in target temperature management at 33 or 36 degrees in the elderly after out-of-hospital cardiac arrest**

M. Winther-Jensen1, T. Fjall2, M. Kiiler3, C. Hassager1, M. Wanscher1, N. Nielsen1, J. Horn1, T. Cronberg1, H. Friberg1, J. Kjaergaard1 on behalf of the TTM steering group.

**Purpose:** Age remains an important determinant of outcome in most cardiac diseases, but the effects of target temperature management (TTM) in elderly survivors of out of hospital cardiac arrest (OHCA) are not well established. We aimed to determine mortality and neurological outcome in elderly comatose OHCA survivors and if age modifies the effect of level of TTM.

**Methods:** This study is a predefined post-hoc analysis of the TTM-trial randomizing 950 patients to 24 h of TTM at 33 or 36 C, which showed no difference in mortality or Cerebral Performance Category (CPC) and modified Rankin Scale (mRS) between the two groups. We analyzed the effect of older age in relation to long term survival and neurological outcome assessed by CPC and mRS after 180 days, dividing patients into 5 age groups: -65 (median), 66-70, 71-75, 76-80 and ≥ 80 years of age.

**Results:** Elderly patients (<65 vs ≥65) more often had no-shockable rhythm (p<0.01), while bystander CPR (p=0.04) and ST-segment elevation ECG were less prevalent (p<0.01). Other pre-hospital characteristics, incl. OHCA location, time to ROSC, witnessed arrest and bystander defibrillation were similar. Increasing age was significantly associated with a lower survival rate (Fig. 1), corresponding to an adjusted hazard ratio (HR) of 1.04 per year of age, 95% CI = 1.04-1.06, p<0.001. As a result, CPC and mRS was higher with increasing age. Surviving on resuscitation, a trend towards worse neurological outcome (CPC=2 or mRS=3) in higher age groups was found (p=0.04, p=0.01, resp.). The effect of level of TTM was not modified by age, Pinteraction=0.94.

**Conclusions:** Increasing age is associated with increased mortality and adverse neurological outcome in comatose survivors of OHCA. There was no difference in outcome between 33 and 36 in any of the age groups.

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**1236 | BEDSIDE**

**Outcome of patients admitted with acute coronary syndrome and given only palliative treatment**

P. Erne1, O. Berte1, P. Urban1, D. Radovanovic1 on behalf of AMIS Plus investigators. 1AMIS Plus Data Center, Institute of Social and Preventive Medicine, University of Zurich, Zurich, Switzerland; 2Hirslanden-Klinik im Park, Zurich, Switzerland; 3La Tour Hospital, Geneva, Switzerland

**Purpose:** At a time when compliance with guidelines is increasingly used to benchmark the quality of hospital care, very little is known about patients admitted with acute coronary syndromes (ACS) who are treated palliatively. This study aimed to evaluate the baseline characteristics and outcomes of these patients.

**Methods:** Using the data of ACS patients enrolled in the AMIS Plus Registry from 1997-2012, characteristics at presentation and outcomes were analysed according to 3 treatment groups: palliative treatment, defined as use of aspirin and analgesics only (no other antiarrhythmics or antplatelets, heparin, vasopressors, intubation, pHb/tilia) and no reperfusion; conservative treatment, defined as any treatment except pharmacological or mechanical reperfusion; and reperfusion treatment (thrombolysis and/or percutaneous coronary intervention during the index admission).

**Results:** Among 39,401 ACS patients, 1367 (3.4%) were treated palliatively, 10,965 (27.8%) conservatively and 27,169 (69.0%) underwent reperfusion therapy. In 1997, 6% of all patients were treated palliatively and 60% conservatively. This continuously decreased to below 3% and 17%, respectively in 2012. In comparison with conservatively treated patients and those who underwent reperfusion, palliative patients were older (77ys vs 72ys vs 63ys; p<0.001), predominantly female (42% vs 35% vs 23%; p<0.001), and suffered more frequently from hypertension (72% vs 65% vs 56%; p<0.001), diabetes (31% vs 25% vs 16%; p<0.001), heart failure (15% vs 8% vs 2%; p<0.001), cerebrovascular diseases (10% vs 11% vs 4%; p<0.001), renal disease (22% vs 15% vs 4%; p<0.001), and dementia (9% vs 6% vs 0.5%; p<0.001). They more frequently required resuscitation prior admission (6% vs 4% vs 4%; p=0.012) and were more often in Killip class III/IV at admission (19% vs 11% vs 5%; p<0.001). Patients treated palliatively had more complications, such as cardiogenic shock after admission (18% vs 8% vs 4%; p<0.001), stroke (17% vs 12% vs 8%; p<0.001) and had a higher hospital mortality than patients treated conservatively or with reperfusion (27.1% vs 11.4% vs 3.5%; p<0.001).

**Conclusion:** ACS patients treated palliatively were older, sicker, with more heart failure diagnosis or admission and suffered a very high in-hospital mortality. While refraining from more active therapy may often constitute the most humane and appropriate approach, a consensus should be reached on whether such patients should be included in the overall evaluation of ACS patient outcomes.

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**Background:** Out-of-hospital cardiac arrest (OHCA) is associated with a poor prognosis and as co-morbidity and susceptibility to critical illness increases with age, ethical dilemmas may arise when OHCA occurs in the very old.

**Methods:** During 2002-2011 consecutive patients with OHCA were treated by the physician-based EMS-system. Pre-hospital data based on Utstein-criteria and data on post-resuscitation care were collected.

**Results:** A total of 5,329 patients with OHCA were recorded, and 24% (n=1,279) were octogenarians. Treatment was more often terminated in the pre-hospital setting in octogenarians (76% vs. 61%, p<0.001), but 218 (16%) octogenarians were successfully resuscitated. Mean age was 85±4 vs 61±12, octogenarians were more often male (54% vs. 74%, p<0.001), whereas non-shockable rhythm (59% vs. 46%, p<0.001) and OHCA in a private setting (73% vs 61%, p<0.001) were more common. Octogenarians were less often treated with therapeutic hypothermia (27% vs. 53%, p<0.001), but cardiac etiology of the OHCA had similar
more than disease management: dilemma in cardiovascular conditions

1248 | SPOTLIGHT
The significance of knowledge and skills of close relatives to patients with LVAD
B. Helmer, J. Graaurup. Rigshospitalet - Copenhagen University Hospital, Heart- and Lung Transplantation, Copenhagen, Denmark

Background: Close relatives to patients with LVAD are often burdened by anxiety regarding malfunction of the LVAD. In order to provide knowledge and skills, an education- and training program has been established at our institution. The aim of this study was to explore the subjective significance of knowledge and skills of close relatives to LVAD patients in order to optimize their training. No similar studies have been identified.

Methods: Qualitative semi-structured interviews with close relatives, living with LVAD patients, to close relatives to patients who had a LVAD between sep. 2011 – mar. 2013 were included, (n=15). Relatives of patients who died, were under the age of 18 or those who were transplanted were subsequently excluded (n=7).

The interviews were recorded and transcribed. Data was divided into two areas; the significance of: “when the close relatives had knowledge and skills” and “when they did not have knowledge and skills”.

Both areas was inductively analysed using U. H. Graneheim and B. Lundman's analysis.

Results: Out of eight possible participants, six (n=6) female spouses participated. The mean age was 56 years (range: 42-63). At the time of the interviews, the patients had in mean had their LVAD for 371 days (range: 43-877).

Where knowledge and skills existed, the data analysis revealed themes which described sense of security, empowerment and psychological well being, but also a feeling of lack of control and experience of negative physiological- and psychological affect. Five of the participants had a desire to know more.

Conclusion: Data analysis revealed that knowledge and skills in relation to the LVAD were of importance to the close relatives. Education and training enhance sense of security, empowerment and add a psychological well being. Where knowledge and skills existed, the data analysis revealed themes which described sense of security, empowerment and psychological well being, but also a feeling of lack of control and experience of negative physiological- and psychological affect. Five of the participants had a desire to know more.

Conclusion: OHCA in octogenarians was associated with a significantly higher mortality rate even after adjustment for other prognostic factors, including comorbidity. However the majority of octogenarian survivors were discharged with a good neurological outcome, and thus refraining from resuscitating the old in general does not seem justified.

1250 | BEDSIDE
An educational intervention nursing at discharge from the emergency department reduces admissions for heart failure in the short term in patients with atrial fibrillation
C. Fuenzalida, I. Ferro, C. Siches, A. Ambros, M. Sanchez, B. Col-Vincent on behalf of the Institute of Biomedical Research August Pi Sunyer (IDIBAPS), Emergency, Barcelona, Spain

Introduction: Atrial fibrillation (AF) is common in the emergency department and has a high morbidity and mortality. An educational nursing intervention can promote self-management for patients and improve their prognosis.

Objectives: To determine whether an educational nursing intervention at discharge from the emergency department reduces admissions for heart failure in the short term in patients with atrial fibrillation.

Material and methods: Clinical, prospective, randomized, blinded and controlled study in AF patients discharged from the emergency department of a tertiary hospital. The trajectory of HF is often unpredictable and it might be relevant to focus on it so far in patients with heart failure (HF). We aimed at (1) assessing associations of health locus of control with HF patient's self-care behaviors and clinical outcomes, and (2) exploring factors associated with the health locus of control in HF patients.

Methods: A total of 107 outpatients with HF (mean age 64, 74% male, 80% NYHA I-II) were followed for 2 years. Health locus of control was assessed with the Japanese health locus of control scale (range: 14-56, a higher score indicates having more internal locus of control). Self-care behaviors were evaluated using the HF self-care risk score (range: 0-6), which was calculated from the European Heart Failure Self-Care Behavior Scale. Depressive symptoms were assessed with the center for epidemiological studies depression scale (CES-D) (range: 0-60). Clinical and demographic data was also collected from the medical chart. Poisson regression model was used to determine if depressive symptoms and control coefficient are associated with the relationship of locus of control with self-care behaviors and clinical outcomes. Multiple regression analysis was used to explore factors associated with the health locus of control.

Conclusion: Social and Welfare Studies, Linköping, Sweden;3 Jonkoping University, School of Health Sciences, Jonkoping, Sweden

Purpose: The trajectory of HF is often unpredictable and it might be relevant to initiate discussions about prognosis with the HF patient by HF nurses. This study aims to describe which subjects Swedish and Dutch HF nurses discuss with their patients concerning prognostic information and why they discuss it. Special focus will be given to the HF patients' interest and why not?

1251 | BEDSIDE
Why do nurses discuss prognosis with the heart failure patient, and why not?
A.-L. Hjelmfors1, M.H. Van Der Wal2, A.S. Stromberg1, M.F. Friedrichsen2, J.M. Martensson3, T.J. Jaarsma2, 1Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden; 2Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden; 3The University of Tokyo, Department of Therapeutic Strategy for Heart Failure, Tokyo, Japan

Purpose: Patients perception of internal locus control (i.e. the belief that health can be improved by one’s own efforts) might be an important factor improving self-care behaviors and clinical outcomes, however only a few studies have focused on it so far in patients with heart failure (HF). We aimed at (1) assessing associations of health locus of control with HF patient's self-care behaviors and clinical outcomes, and (2) exploring factors associated with the health locus of control in HF patients.

Methods: A total of 107 outpatients with HF (mean age 64, 74% male, 80% NYHA I-II) were followed for 2 years. Health locus of control was assessed with the Japanese health locus of control scale (range: 14-56, a higher score indicates having more internal locus of control). Self-care behaviors were evaluated using the HF self-care risk score (range: 0-6), which was calculated from the European Heart Failure Self-Care Behavior Scale. Depressive symptoms were assessed with the center for epidemiological studies depression scale (CES-D) (range: 0-60). Clinical and demographic data was also collected from the medical chart. Poisson regression model was used to determine if depressive symptoms and control coefficient are associated with the relationship of locus of control with self-care behaviors and clinical outcomes. Multiple regression analysis was used to explore factors associated with the health locus of control.

Conclusion: The significance of knowledge and skills of close relatives to patients with LVAD patients was 81% vs. 55% (p<0.001), Fig.1, which remained significant after adjustment for known confounders (HR=1.68 (95%CI: 1.34-2.10), p<.001). A favorable neurological outcome (cerebral performance category 1 or 2) was found in 72% (n=33) of octogenarian patients compared to 85% (p=0.02) corresponding to an adjusted OR 0.28 (CI 0.11-0.75), p<.01.

Conclusion: OHCA in octogenarians was associated with a significantly higher mortality rate even after adjustment for other prognostic factors, including comorbidity. However the majority of octogenarian survivors were discharged with a good neurological outcome, and thus refraining from resuscitating the old in general does not seem justified.

MORE THAN DISEASE MANAGEMENT: DILEMMA IN CARDIOVASCULAR CONDITIONS

1249 | BEDSIDE
Health locus of control and self-care and their role in clinical outcomes in patients with heart failure
1Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden; 2The University of Tokyo, Department of Cardiovascular Medicine, Tokyo, Japan; 3The University of Tokyo, Department of Therapeutic Strategy for Heart Failure, Tokyo, Japan

Purpose: Patients perception of internal locus control (i.e. the belief that health can be improved by one’s own efforts) might be an important factor improving...
1252 | BEDSIDE
Sleep quality and quantity: association with quality of life and function in patients with pulmonary hypertension
M.C. Deaton1, I. Armstrong2, M. Campbell3, L. Mcgowan4, P. Sephton2

Aim: Although sleep apnoea is prevalent in patients with pulmonary hypertension (PH), few studies have evaluated sleep quality and quantity and its effect on patient well-being. The aim of this analysis was to determine the effect of sleep on quality of life, fatigue and function in patients with PH.

Methods: As part of a longitudinal study the following baseline data were collected: demographic and clinical information, 6 minute walk distance (6MWD), functional class (FC) rated by clinician and patient, and questionnaires: MOS EmPHasis-10, FSS, patient and clinician rated somnolence and SPI subscales reported fewer hours of sleep, more fatigue and worse function and normal LV systolic function. The CHF was defined as elevated serum BNP, more than 162 msec might help us to predict the new onset CHF.

Results: During a HF clinic visit, discussing prognosis occurs less often than discussing other topics such as HF symptoms or adherence. Prognosis is not always seen as the most important subject to discuss. A change in patient condition is an important reason for nurses to discuss prognosis. This information can be used to help nurses find an optimal time and opportunity to discuss prognosis with HF patients.

Conclusions: A paced QRS duration could predict the new-onset congestive heart failure after permanent right ventricular apical pacing in patients with acquired high-grade atrioventricular block and normal left ventricle.

A paced QRS duration could predict the new-onset congestive heart failure after permanent right ventricular apical pacing in patients with acquired high-grade atrioventricular block and normal left ventricle (LV) dysfunction and contributes to the development of heart failure (HF). A paced QRS duration and echocardiographic parameters between LV systolic dysfunction and normal LV systolic function. The CHF was defined as elevated serum pro-BNP level (more than 700 pg/dl) or CHF hospitalization.

Results: The mean follow up duration was 76 months. The permanent RV apical pacing was associated with the new-onset CHF in 42 patients (18%) with high degree AV block. In multivariate analysis, after adjusting age, sex, LV EF, the history of hypertension and CAD, pacing duration, and medication, a paced QRS duration could independently predict the new-onset CHF. A paced QRS duration more than 162 msec might help us to predict the new-onset CHF.

Conclusions: A paced QRS duration might be associated with the new-onset CHF after permanent RV apical pacing in patients with high degree AV block. So, we try to decrease the paced QRS duration in permanent RV apical pacing.

1263 | BEDSIDE
Erectile function in ICU patients
P.P. Johansen1, A.D. Zwister2, M.L. Rasmussen3, J.H. Svendsen4, M. Frederiksen1, J.K. Bae, S.P. Hong, J.B. Lee, J.K. Ryu, J.Y. Choi, K.S. Kim, S.G. Chang, Catholic University of Duesseldorf, Department of Cardiology, DUCMC, Daegu, Korea, Republic of

Purpose: The right ventricular (RV) apical pacing results in progressive left ventricular (LV) dysfunction and contributes to the development of heart failure (HF). In a 210, 7.9 mild erectile dysfunction (Score range 22 to 25) and 36.1 having no erectile dysfunction (Score range 26 to 30). Mean score for Orgasmic Function domain was 6.2±4.2 (Score range 0 to 10). Sexual Desire domain was 6.3±2.5 (Score range 2 to 10), and Intercourse Satisfaction domain was 6.4±5.6 (Score range 0 to 15) and Overall Satisfaction domain was 6.3±2.6 (Score range 2 to 10).

Conclusions: Erectile dysfunction was present in more than 60% of male patients with implantable cardioverter defibrillator and more than 40% had severe erectile dysfunction. Also intercourse satisfaction was affected. All though this is not conclusive, results indicates that sexual function needs to be addressed in patients with implantable cardioverter defibrillator.

INNOVATIONS IN CARDIAC PACING

1269 | BEDSIDE
Sleep quality and quantity: association with quality of life and function in patients with pulmonary hypertension
M.C. Deaton1, I. Armstrong2, M. Campbell3, L. Mcgowan4, P. Sephton2, J. Yorke5, 1 University of Cambridge, Institute of Public Health, Department of Public Health and Primary Care, Cambridge, 2 Pulmonary Hypertension Association, Sheffield, 3 University of Manchester, Manchester, 4 University of Leeds, School of Healthcare, Leeds, United Kingdom

Aim: Although sleep apnoea is prevalent in patients with pulmonary hypertension (PH), few studies have evaluated sleep quality and quantity and its effect on patient well-being. The aim of this analysis was to determine the effect of sleep on quality of life, fatigue and function in patients with PH.

Methods: As part of a longitudinal study the following baseline data were collected: demographic and clinical information, 6 minute walk distance (6MWD), functional class (FC) rated by clinician and patient, and questionnaires: MOS EmPHasis-10, FSS, patient and clinician rated somnolence and SPI subscales.

Results: Sleep quality had stronger associations than sleep quantity with quality of life, fatigue and patient function. Use of sleep questionnaires may be a simple method to identify patient difficulties and highlight patients who need further investigation. Subsequent studies should incorporate sleep monitors to enhance understanding of sleep and its effects on well-being in patients with PH.

Conclusions: Sleep quality had stronger associations than sleep quantity with quality of life, fatigue and patient function. Use of sleep questionnaires may be a simple method to identify patient difficulties and highlight patients who need further investigation. Subsequent studies should incorporate sleep monitors to enhance understanding of sleep and its effects on well-being in patients with PH.
1264 | BEDSIDE

Left anterior descending coronary artery flow impaired by right ventricular apical pacing and its relevance to pacing-induced systolic dyssynchrony

F. Fang1, Z.N. Jin2, P.W. Lee1, J. Sanderson3, H.Y. Li4, W.J. Zhang5, Z.A. Li6, Y. Yang5, X.X. Luo1, C.M. Yu1. 1The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China; 2Public of 2Beijing Anzhen Hospital, Capital Medical University, Beijing, China; 3People’s Republic of China

Introduction: Although right ventricular apical (RVA) pacing may affect the coronary blood flow; however, there is no prospective study to address. We aimed to assess coronary blood flow changes after RVA pacing and the role of systolic dyssynchrony.

Methods: Seventy patients with sinus node dysfunction were prospectively enrolled. Coronary flow was evaluated by diastolic velocity time integral (VTI) at the distal-port of left anterior descending coronary artery (LAD) with transhoracic echocardiography at baseline and follow-up. Systolic dyssynchrony was assessed with tissue Doppler imaging by time standard deviation to peak systolic velocity of 12 left ventricular segments (cutoff value ≥33ms).

Results: Sixty-five patients were finally analyzed. At follow-up (mean time: 127±45 days), LAD velocity-time integral (LAD-VTI: 12.1±4.2 vs. 10.7±4.6 cm³, p<0.001) were decreased together with left ventricular systolic deterioration (ejection fraction: 65±7% vs. 62.1±7%, p=0.05). However, these changes were only detected in those with pacing induced systolic dyssynchrony (Table). Significantly, LAD-VTI reduction (defined as ≥5%) occurred in 34 (52%) patients which was more prevalent in pacing-induced systolic dyssynchrony group (83.5% vs. 16.5%, p<0.001). Though similar at baseline, LAD-VTI was significantly lower in dyssynchrony group at follow up (p<0.001). Cox-regression analysis showed that pacing inducing systolic dyssynchrony (hazard ratio (HR): 3.62, p<0.05) and accumulative pacing percentage >40% (HR: 3.32, p<0.027) were associated with LAD-VTI reduction. In multiple analysis, only pacing inducing systolic dyssynchrony was the associated factor (HR: 2.93, p=0.045).

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1265 | SPOTLIGHT

Clinical utility and effects on patients outcome of pacemaker remote follow-up: single center experience of 2000 patients

O. Al-Razo, E. Gonzalez Villegas, M. Alejandre, T. Represa, J.M. Mesa. Hospital University La Paz, Department of Cardiac Surgery, Madrid, Spain

Introduction: In spite of the fact that several studies have demonstrated the feasibility and technical reliability of pacemaker (PM) remote follow-up, Physicians are still reluctant to use it as the method of choice for PM follow-up. In this study we report our 6 years experience in PM remote follow-up and the impact of using this technology on patient medical care and health resource utilization.

Patients and methods: Two thousands patients with PM were included in the remote follow-up clinic between February 2008 and February 2014. The clinic was managed by 2 pacing expert nurses, 2 physicians and the head of the unit. Fifty minutes/week for the nurse and 15 min/week for the physician were spent for remote follow-up data analysis.

After the third month post PM implant, the patients were completely followed-up by the remote follow-up clinic.

Results: 164 (8.2%) complications were reported, the majority were corrected by phone calls (95%), and the rest, with a visit to the PM follow-up clinic. In 5 (0.3%) patients, the monitor had to be replaced due to dysfunction. 99.8% of patients were completely satisfied with the remote follow-up of their pacemakers according to a survey that was conducted to all the patients and only 4 (0.2%) were willing to return to out-patient visits due to personal demand.

Arrhythmia (atrial fibrillation and/or atrial tachycardia) was the most frequent alert (14%). In 66 patients new onset atrial fibrillation was diagnosed. There were 22 (1,1%) alerts for ventricular tachycardia; only in 2 cases were proved to be true. Thirty alerts for lead dysfunction were received, 53% of which were due to lead impedance changes. Fourteen cases of lead displacement were diagnosed and one case of rupture of lead insulation.

The PM remote follow-up unit in our department reduced the workload on our out-patient PM clinic by 46%.

Conclusions: This study confirms that PM remote follow-up is feasible and reliable. It helps in early detection of lead problems and arrhythmias and plays a role in the optimization of health-care resource allocation.

1266 | BEDSIDE

A leadless pacing device, first in-humana data on feasibility and safety

C. Eitel, M. Doering, S. John, P. Sommer, O. Breithard, S. Richter, G. Hindricks. University of Leipzig, Heart Center, Leipzig, Germany

Purpose: Leadless pacing devices have recently been developed to overcome the limitations of conventional pacemakers with respect to lead and device pocket associated complications. We report initial clinical experiences of the first 5 patients implanted at our hospital.

Methods: From November 2013 until January 2014, 5 patients with conventional 1-chamber-pacemaker indication underwent implantation of a leadless pacing device. Device implantation was performed with a minimally invasive approach using the right femoral vein for vascular access. Procedural data, device performance and complications during as well as after the implantation procedure were assessed.

Results: The device could be implanted successfully in all patients (mean age 78.4±6.0 years) in the apiocardial region of the right ventricle. In 4/5 patients sensing and pacing values were acceptable at the first implantation site, while in one patient the device had to be repositioned once due to impaired sensing values. Two periprocedural complications occurred with one patient with pre-existing LBBB experiencing temporary completely anterioatrial block during manipulation with the catheter delivery system and one patient suffering from a pseudoaneurysm of the right femoralis profundus that could be treated with thrombin injection. Device parameters at discharge were stable in all patients.

Procedural data

<table>
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<th>Patient</th>
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</tr>
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<td>3</td>
<td>50</td>
<td>10.5</td>
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<td>-</td>
</tr>
<tr>
<td>4</td>
<td>80</td>
<td>16.5</td>
<td>1352</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>7.2</td>
<td>807</td>
<td>Pseudoaneurysm of the right femoral artery</td>
</tr>
</tbody>
</table>

1 | *P<0.05 vs. the corresponding column of no systolic dyssynchrony group.

Conclusions: In this small patient series implantation of a leadless pacing device was successful in all patients with good sensing and pacing values. Lack of a subcutaneous device pocket and permanent leads is particularly attractive due to a potential reduction of device and lead associated complications. Data on long-term performance and safety are needed.

1267 | BEDSIDE

A leadless cardiac pacemaker: single center 18 months follow-up results

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Purpose: Transvenous and epicardial leads have been the standard for patients with pacemaker systems for over 50 years. A novel completely self-contained Leadless Cardiac Pacemaker (LCP) has been introduced to reduce complications associated with lead placement, lead performance and the subcutaneous pulse generator. We evaluated the clinical performance of this device in patients with a minimum of 1-year follow-up.

Methods: Patients with an indication for VVI-pacing were considered for enrolment. Eligible patients were implanted with a LCP. Under fluoroscopic guidance the LCP was inserted through the femoral vein using an 18Fr delivery catheter. The LCP was positioned in the right ventricular apex, fixated using a screw-in helix, and released after obtaining satisfactory electrical measurements. All consecutive patients with a LCP implanted in our center between Dec 2012 and Mar 2013 were included.

Results: A total of 8 patients (82±9 years, 75% male) were implanted with a LCP. The implant success rate was 100% with a mean procedure time of 41±17 minutes (range, 24 to 67 minutes). In patients enrolled the complication-free rate was 100%. One patient did not complete follow-up due to the need for ICD-implantation and successful LCP retrieval. The pacing performance results at implant, discharge, 3 and 9 months follow-up were respectively: mean threshold at 0.4 ms pulse width; 0.79±0.49 V, 0.39±0.13 V, 0.43±0.19 V, 0.41±0.17 V, R-wave amplitude; 7.3±3.9 mV, 8.4±7.8 mV, 9.3±5.1 mV, 9.7±3.0 mV, impedance; 873±281 Ohms, 824±158 Ohms, 739±207 Ohms, 690±188 Ohms. There were no late complications. At the time of this data set compilation, 14 Feb 2014, not all subjects have had their 18 months post-implant follow-up visit to allow us to evaluate the clinical performance of the LCP at 18 months. Performance and safety results at 18 months will be updated later and added to this analysis.

Conclusions: In our center this novel Leadless Cardiac Pacemaker demonstrates very stable performance and safety results during follow-up. We here present the longest follow-up results of the performance of the LCP to date. Our results support the use of the LCP as a safe and reliable alternative to conventional pacemaker systems. Continued evaluation is warranted to further characterize this system.
2.45, p=0.0001; AUC observed with the AUC tertiles. More had glucose intolerance or a metabolic syndrome. A similar association was est tertile (mance by optimising this first-generation prototype.

Results: A harvesting device was derived from the clockwork of an automatic wristwatch. The harvester was then anchored on the heart thanks to a custom-made housing (total mass 16.7 g, figure). For an in-vivo study with a 60 kg domesticated pig, a sternotomy was performed to suture the prototype onto the anterolateral part of the left ventricle. The harvesting device was connected to a custom-built single-chamber pacemaker. Finally, an epicardial bipolar pacing wire was used to deliver the pacemaker stimulus.

Methods: The energy harvesting device supplied the pacemaker with enough energy to perform continuous VVI pacing (pacing threshold 0.0 V/0.5 ms, sensing 9.8 mV, impedance 1279 Ω) at 130 bpm (pacing output 1.6 V/0.8 ms). Simultaneously, the harvesting device generated a mean output power of 52 μW over an additional lead resistor of 1 kΩ.

Conclusion: We demonstrated the feasibility of pacing the heart using its own mechanical activity. The harvested energy exceeded the power requirement of a modern pacemaker (~10 μW). Furthermore, we expect to increase the performance by optimising this first-generation prototype.

Poster Session 2

LIPOPROTEINS IN CARDIOVASCULAR PREVENTION

P1270 | BEDSIDE

Triglycerides are independent risk predictors in stable coronary artery disease

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Objective: Risk prediction with fasting compared to postprandial serum triglycerides (TG) in patients with cardiovascular disease remains unclear, especially in patients who are treated with a statin. The aim of this prospective study was to analyze the role of fasting and postprandial serum triglycerides (TG) as risk modifiers in patients with coronary artery disease (CAD).

Methods: A sequential oral triglyceride (OTT, 75g cream fat) and glucose tolerance test (OGT, 75g glucose) was applied to obtain standardized measurements of postprandial TG glucose kinetics in patients with stable CAD confirmed by angiography. Lipid and glucose parameters were measured at fasting, 3, 4, and 5 hours after the OGGT. The primary outcome was the composite endpoint of death and hospitalization for acute coronary syndrome or hospitalization for unplanned, symptom-induced coronary angiography and revascularization within 48 months follow-up.

Results: N=514 patients with angiographically confirmed, clinically stable CAD were enrolled. Median age was 68 years, 83% were male, 95% were treated with statins and median LDL-cholesterol concentration was 150mg/dl. Fasting TG were strongly associated with the area under the curve (AUC) of the postprandial TG increase (R=0.93, p<0.0001). Patients were stratified by TG tertiles for statistical comparisons of baseline variables and time-to-event analyses. Compared to the lowest tertile of fasting TG (<106mg/dl), patients in the high-est tertile (>150mg/dl) were younger, more obese, more were smoking, they had a higher blood pressure and pulse, lower HDL- and higher LDL-cholesterol and more had glucose intolerance or a metabolic syndrome. A similar association was observed with the AUC tertiles. Follow-up at was 100% complete. Both fasting and postprandial TG predicted the primary outcome (fasting TG >150mg/dl vs. <106mg/dl: HR 1.79, 95%-CI 1.31-2.45, p=0.0001; AUC >1120mg/dl vs. <750mg/dl: HR 1.78, 95%-CI 1.29-2.45, p=0.0003). Postprandial TG parameters did not improve risk prediction compared to fasting TG. The number of cardiovascular deaths and myocardial infarctions was higher in the upper tertile of fasting TG ~150mg/dl (HR 1.79, 95%-CI 1.04-3.09, p=0.03). Risk prediction by TG was independent of traditional risk factors, medication, glucose metabolism, LDL- and HDL-cholesterol.

Conclusions: Fasting serum triglycerides ~150 mg/dl independently predict cardiovascular events in patients with coronary artery disease on guideline-recommended medication. Assessment of postprandial TG does not improve risk prediction compared to fasting TG in these patients.

P1271 | BEDSIDE

Impact of statin therapy on low-density lipoprotein cholesterol and triglyceride levels in patients with hypertriglyceridaemia: a VOYAGER meta-analysis

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Background: Several studies have indicated a causal role for triglycerides (TG) in the development of coronary artery disease. Recently published guidelines from the European Atherosclerosis Society (EAS) Consensus Panel define mild-to-moderate hypertriglyceridaemia as a TG level of 2.0–10.0 mmol/L and recommend a TG level <1.7 mmol/L as desirable; however, the primary treatment goal in these patients remains the LDL-C goal. Individual patient data (n=32,258) from the VOYAGER meta-analysis of 37 studies were used to analyse LDL-C and TG reduction in patients with baseline TG >2.0 mmol/L.

Methods: The least-squares mean (LSM) % change from baseline in LDL-C and TG was compared during 15,800 patient exposures to rosuvastatin (RSV) 5, 10, 20 and 40 mg, atorvastatin (ATV) 10, 20, 40 and 80 mg, and simvastatin (SIM) 10, 20, 40 and 80 mg in patients with baseline TG >2.0 mmol/L. Comparisons were made using a single mixed-effects model using only data from studies directly comparing treatments by randomised design.

Results: LSM % reductions in LDL-C and TG are shown in the figure. Reductions in LDL-C with RSV 10–40 mg were significantly greater than for equal or double doses of ATV and SIM (all p<0.05). RSV 10 mg produced a significantly greater (p<0.05) reduction in TG than ATV 10 mg, but reductions with RSV 20 and 40 mg were similar to equal doses of ATV. Doses of RSV 10–40 mg resulted in significantly greater (p<0.05) reductions in TG than equal or double doses of SIM.

Conclusions: In patients with hypertriglyceridaemia, LDL-C reduction, the primary treatment goal, was substantial and dependent on the choice and dose of statin. The reduction in TG was numerically less than for LDL-C, and additional therapy may be considered to potentially further reduce residual cardiovascular risk.
Methods: A total of 264 patients in our hospital were enrolled. Biochemical markers for lipid metabolism including serum apo-48, TG, LDL-C, HDL-C and proteinuria were measured. Subjects were classified into 4 groups by eGFR and proteinuria: high eGFR (>60 mL/min/1.73 m²) without proteinuria (≥1+ by urine dipstick) (n=50); high eGFR with proteinuria (n=73); low eGFR (>60 mL/min/1.73 m²) without proteinuria (n=74); and low eGFR with proteinuria (n=65). ApoB-48 level and apoB-48/TG ratio were compared among these groups and multiple regression analysis was done using these parameters.

Results: Serum log-apo-48 and log-apo-48/TG levels were significantly higher in patients with low eGFR without proteinuria, low eGFR with proteinuria and low eGFR without proteinuria than in those with high eGFR without proteinuria. eGFR was significantly correlated with log-apo-48 and log-apo-48/TG levels, but urine protein level was significantly correlated only with the log-apoB-48 level. Multiple regression analysis indicated that log-apoB-48/TG levels were a significant determinant of reduced eGFR, suggesting that increased serum apoB-48 concentrations partly contributed to an increased risk of CKD.

Conclusion: Both low eGFR (<60) and proteinuria (≥1+) were independent determinants of high apoB-48 levels. Taken together, the present results suggest that increased serum apoB-48 concentrations may contribute to an increased risk of cardiovascular events.

P1273 | BENCH
Precise non invasive diagnosis of subclinical and mild coronary artery disease promotes the rationale use of statins and very low outcomes in hypercholesterolemic patients
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Background: Statin therapy is one of the cornerstones of prevention of cardiovascular (CV) events in patients (P) with hypercholesterolemia (HC). It is controversial the impact of the diagnosis of subclinical and mild coronary artery disease (CHD) in the prescribing of a statin and subsequent outcomes in P with HC.

Aim: To analyze changes in statin use and outcomes after the non invasive diagnosis of subclinical and mild coronary artery disease (CHD) in the prescribing of a statin and subsequent outcomes in P with HC.

Methods: Prospective and observational study of a cohort of 400 P screened between 2007 and 2009, without cardiovascular history and submitted to diagnose CHD by means of non invasive coronary angiography using 64-rows multidetector CT (MDCT). Current Appropriateness Criteria and Guidelines for the diagnosis of CHD and the performance of MDCT were strictly observed, including blinded CT review. Main variables included were age, sex, major risk factors, CHD status (normal coronary arteries or mild CHD with luminal stenosis <50%), drugs (statin, aspirin, ACE inhibitor, ARB, Calcium channel antagonists, diuretic and betablocker) and outcome (total mortality, cardiovascular mortality, non fatal MI, unstable angina, PCI or CABG). The follow up, CV outcomes collection and pre-scribing propensity was accomplished through historic controls from Euroaspeire Survey and medical records and data collected from a wide Community Database jointly managed by care centers and general practitioners. The MDCT report did not add advices or recommendations over any drug prescription.

Results: After a median of 4.6 years, a total of one hundred and forty six P completed the survey: mean age 63±13 yo; M/F ratio 45/55. Prevalence of HC was 41% and subclinical and mild CHD was diagnosed in 49%. After the follow up, in HC group, statin prescription was 50% when the diagnosis was of normal coronary arteries, increasing to 84% when the diagnosis was subclinical and mild CHD (Odds Ratio 3.9; 95% CI 1.2-23.1: p=0.02). Hence, the prescription propensity after MDCT resulted in 5 vs. 3 additional treatments with statin per 100 patients-years compared with hypercholesterolemic P and normal coronary arteries. Outcomes were very low and similar to P with normal coronary arteries (0.3 vs. 0.5 major events per 100 patients-years).

Conclusion: Non invasive diagnosis of subclinical and mild CHD; 1) increase the prescription of a statin in hypercholesterolemia; 2) enhancing the adherence to evidence based preventive therapies resulted in a very low incidence of major CV events at long term follow up.

P1274 | BENCH
Anti-TNF therapy improves endothelial protective functions of HDL in patients with rheumatoid arthritis
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Purpose: Recent studies suggest that HDL may adopt a pro-atherogenic phenotype in patients with rheumatoid arthritis (RA). However, the effects of common anti-inflammatory treatments on HDL function are not yet known. In this study we investigated the impact of infliximab + methotrexate (MTX) versus placebo + MTX on HDL functionality in patients with early RA.

Methods: Eighteen patients 55.58 (12.45) years with erosive early RA receiving MTX were randomised to infliximab (3mg/kg) or placebo infusion. At week 54 and thereafter, all patients received infliximab. HDL function was measured at baseline, 54 weeks and 110 weeks. The impact of HDL on cultured endothelial cells was assessed using ESR Spectroscopy for nitric oxide bioavailability (NO) and Superoxide Production (SO). HDL-associated Paraoxonase-1 (PON-1) activity was measured by spectrophotometry. HDL-mediated cholesterol efflux was measured in J774 macrophages, pre-treated with cAMP.

Results: Combination of infliximab and MTX treatment at 54 weeks resulted in significantly improved HDL endothelial properties compared to MTX alone. At 110 weeks, following two years treatment with Infliximab and MTX all endothelial HDL properties including NO, SO and PON-1 were significantly improved (p<0.01) (Fig. 1). HDLs cholesterol efflux capacity remained unchanged at 54 and 110 weeks of treatment.

P1275 | BEDSIDE
Anti-enzyme inhibitor of apoC-III produces significant decreases in apoC-III and triglycerides and increases in HDL-C as a single agent or in combination with fibrates in hypertriglyceridemic patients
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Background: ApoC-III is a 79 amino acid glycoprotein, synthesized principally by the liver, which associates with apoB-containing lipoproteins and HDL. It plays a pivotal role in regulating plasma triglyceride (TG) levels by inhibiting hydrolysis of TG-rich lipoproteins as well as receptor-mediated uptake of lipoprotein remnants by the liver and is recognized as a CV risk factor. ISIS-APOCIIIRx selectively inhibits apoC-III protein synthesis in the liver.

Purpose: To assess the change from baseline in fasting lipids and lipoproteins following 13 weeks of treatment with ISIS-APOCIIIRx as a single agent or in combination with fibrates in patients with hypertriglyceridemia (HTG).

Methods: Patients ≥18 years were enrolled in double-blind Phase 2 studies to receive ISIS-APOCIIIRx (up to 300 mg) or placebo as weekly SC injections for 18 years were enrolled in double-blind Phase 2 studies to receive ISIS-APOCIIIRx (up to 300 mg) or placebo as weekly SC injections for 13 weeks. Patients were randomized to one of four groups: 1) placebo + placebo; 2) placebo + placebo; 3) ISIS-APOCIIIRx + placebo; 4) ISIS-APOCIIIRx + placebo. Patients were ≥18 years and had fasting TGs ≥500 mg/dL. Patients received the ISIS-APOCIIIRx or placebo as a single SC injection weekly for 12 weeks and then received an additional SC injection at week 13. The primary endpoint was percentage change from baseline in fasting TG levels at week 13.

Results: Treatment with ISIS-APOCIIIRx resulted in consistent and significant decreases in fasting TGs and triglycerides and increases in HDL-C as a single agent or in combination with fibrates in hypertriglyceridemic patients.

Table 1

Fasting triglycerides (mg/dL) Mean % (SD) change from baseline

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean baseline (mg/dL)</th>
<th>Week 13 (mg/dL)</th>
<th>% change (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>359 ±140</td>
<td>359 ±140</td>
<td>0% (0-6)</td>
</tr>
<tr>
<td>ISIS-APOCIIIRx</td>
<td>529 ±139</td>
<td>239 ±139</td>
<td>-53% (18.1)</td>
</tr>
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</table>

* p<0.001 ** p<0.01 *** p<0.001.
Lipoproteins in cardiovascular prevention

P1276 | BEDSIDE
Systematic study of the effects of lowering low-density lipoprotein-cholesterol on regression of coronary artery diseases using intravascular ultrasound
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Objective: Conflicting results currently exist on the effects of LDL-C levels on coronary atherosclerotic plaque, and the target level of LDL-C resulting in the regression of the coronary atherosclerotic plaques (CAP) has not been settled.

Methods: PubMed, EMBASE, and Cochrane databases were searched from Jan. 2000 to Nov. 2013 for randomized controlled or blinded end-point trials assessing the effects of LDL-C lowering therapy on regression of coronary atherosclerotic plaque in patients coronary heart disease by intravascular ultrasound. Data concerning the study design, patient characteristics, and outcomes were extracted. The significance of plaques regression was assessed by computing standardized mean difference (SMD) between the baseline and follow-up. SMD were calculated using fixed or random effects models.

Results: Twenty trials including 5910 patients with coronary heart disease were identified. Lowering LDL-C by >45% and to a target level ≤66.8 mg/dL in baseline LDL-C >120 mg/dL was associated with a greater reduction of volume of CAP as compared to LDL-C levels below 4 mmol/L. The 2012 ESC guidelines recommend a LDL-cholesterol (LDL-C) of <3.4 mmol/L in patients with coronary heart disease, and the target level of LDL-C was <1.8 mmol/L.

Conclusion: LDL-C levels ≤3.9 mmol/L were associated with increased regression of coronary atherosclerotic plaque.

P1277 | BEDSIDE
Phytosterol and oxyphytosterol levels in plasma and aortic valve cusps in patients with severe aortic stenosis
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Background: We hypothesized that in patients with severe aortic stenosis phytosterols and oxyphytosterols (sitosterol, campesterol and desmosterol) were increased in arterial and aortic valve cusps correlating with each other, independent of statin treatment.

Methods and results: We included 104 consecutive patients (68/36; m/f) between 40 and 87 years (mean 69.8±6.3) who were admitted to our hospital for elective aortic valve replacement because of severe aortic stenosis. Study participants were assessed for established cardiovascular risk factors and concomitant statin treatment (no statins: 36/statins: 68). Venous blood samples were drawn one day prior valve surgery and the aortic valve cusp samples were analyzed to determine non-cholesterols (cholesterol, lathosterol, lanosterol and desmosterol) and phytosterols (7α-OH, 7β-OH, 7 keto-campesterol, -sitosterol) by gas chromatography-flame ionization mass spectrometry. As expected, there were significantly lower absolute and cholesterol corrected serum concentrations of cholesterol precursors (lathosterol, lanosterol and desmosterol) in statin treated patients. The concentration of the two most common plant sterol (sitosterol and campesterol) strongly correlated with each other and in plasma (r=0.911; p=0.0001) and aortic valve cusp concentrations (r=0.945; p=0.0001) as well as between the two groups (r=0.488; p=0.0000 campesterol; r=0.350; p=0.0001 sitosterol). We found a significantly increased concentration of sitosterol in plasma and aortic valve cusps (r=0.712; p=0.0000 campesterol to sum oxy sterol; r=0.706; p=0.0000 sitosterol to sum oxy sterol), but not in serum (r=0.243; p=0.014 campesterol to sum oxy sterol; r=0.317; p=0.0001 sitosterol to oxy sterol). Furthermore, there was a significant correlation between 7α-hydroxy-, 7β-hydroxy- and 7 keto-campesterol/sitosterol in aortic valve tissue, irrespective of statin treatment.

Conclusion: In patients with severe aortic stenosis phytosterols and their respective metabolites were significantly increased in arterial valve tissue, but not in serum. Moreover, there is no correlation of oxyphytosterols in serum with their respective concentrations in aortic valve cusps. These data suggest that sterol oxidation in cardiovascular tissue is a local process that is independent of statin treatment.

P1278 | BEDSIDE
The influence of statin intake on the progression of the coronary artery calcification: the Heinz Nixdorf Recall study
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Purpose: Statin intake is regarded to stabilize coronary artery plaques. We aimed to determine, whether this influences the progression of coronary artery calcification (CAC).

Methods: Participants from the Heinz Nixdorf Recall Study (age 45 to 75 years) with known coronary cardiovascular disease were included. CAC was assessed using electron beam computed tomography at baseline and after five years and quantified by the Agatston Score. Regression analysis was used to determine the association of CAC progression with statin intake with Log- transformation of CAC to normalize for its distribution. CAC progression was defined as difference of log-transformed CAC (log[CAC(t+5)]-log[CAC(0)]).

Results: Overall, 3483 subjects (mean age 59 years, 47% male) were included. Subjects with statin intake had higher CACS at baseline (median [Q1; Q3]: 58 [26; 273; 233] vs. 5.9 [0; 9.2], p<0.0001) and higher absolute CAC progression over 5 years (median [Q1; Q3]: 57.1 [4.6; 256.0] vs. 7.7 [0; 83.3], p<0.0001). In unadjusted regression analysis, statin intake was associated with higher CAC progression (Estimate [95% confidential Interval]: 39 [20-62%], p<0.0001) with a similar effect size when adjusted for cardiovascular risk factors including cholesterol levels (31 [12-52%], p<0.0006).

Conclusion: Within the 5 years follow-up, statin intake was associated with increased progression of CAC in the general population without known cardiovascular diseases despite their lipid lowering effect, confirming the trend, suggested in previous randomized clinical trials. Notwithstanding other explanations like bias by indication, our results may support the hypothesis of a plaque stabilizing effect of statins, which might be reflected by an increase in CAC.
associated with an increased all cause mortality (HR 1.72; 95% CI [1.17-2.54], p<0.05) as well as LDL-C <6 mmol/L (HR 2.60; 95% CI [1.49-4.85], p<0.001).

**Conclusions:** LDL-C levels higher than 4 mmol/L were significantly associated with all-cause and cardiovascular mortality in primary prevention. The observation of a gradient of risk associated with elevated LDL-C supports causality in this low risk population. The 2012 ESC LDL-C target seems to be appropriate in Southern Europe.

**P1280 | BEDSIDE**

Association of a polymorphism of the zinc finger protein 259 gene (ZNF259) with dislipidemia in Japanese individuals

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**Purpose:** Various loci and genes that confer susceptibility to coronary heart disease (CHD) have been identified for Caucasian populations by genome-wide association studies (GWASs). Given that dyslipidemia is a major risk factor for CHD, we hypothesized that some polymorphisms might contribute to the genetic susceptibility to CHD through affecting the susceptibility to dyslipidemia. The purpose of the present study was to examine the possible association of dyslipidemia (hypertriglyceridaemia, hyper-HDL-cholesterolaemia, or hyper-LDL-cholesterolaemia) in Japanese individuals with 15 polymorphisms identified as susceptibility loci for CHD in the previously GWASs.

**Methods:** Study subjects comprised 5460 Japanese (2354 subjects with dyslipidemia, 3106 controls) who visited the participating hospitals between 2002 and 2010. Dyslipidemia was defined as a serum triglyceride of >1.65 mmol/L, a serum HDL-cholesterol of <0.91 mmol/L, or a serum LDL-cholesterol of >3.46 mmol/L. To compensate for multiple comparisons, we adopted the criterion of a false discovery rate (FDR) of 0.05 for statistical significance of association.

**Results:** Comparisons of allele frequencies by the chi-square test revealed that the rs964184 of the zinc finger protein 259 gene (ZNF259) was significantly (P=0.0006, FDR=0.0094) associated with dyslipidemia. Multivariable logistic regression analysis with adjustment for age, sex, and body mass index revealed the rs964184 of ZNF259 was significantly associated with dyslipidemia (P=0.0029; odds ratio, 1.25; dominant model) were significantly associated with dyslipidemia (P=0.0029; odds ratio, 1.25; dominant model) were significantly associated with dyslipidemia.

**Conclusions:** Association of a polymorphism of the zinc finger protein 259 gene (ZNF259) with dislipidemia in Japanese individuals.
gusted to play an important role in cardiac remodelling, hypertrophy, immune response and inflammatory signalling. Yet data on its potential clinical relevance as a predictor for cardiovascular disease (CVD) events and mortality are controversial. Thus, we assessed the predictive value of sST2 for subsequent CVD events and total mortality in stable coronary heart disease (CHD) patients, simultaneously controlling for a large number of potential confounders.

**Methods:** Plasma concentrations of sST2 (ELISA, Critical Diagnostics) were measured at baseline in a cohort of 1,073 patients aged 30-70 years with stable CHD. The Cox proportional hazards model was used to determine the prognostic value of sST2 concentrations for cardiovascular endpoints.

**Results:** The median sST2 level was 28.9 ng/mL (IQR 23.8, 35.1). Elevated sST2 levels were associated with male gender and left-ventricular dysfunction but not with age, history of hypertension, and heart failure. Furthermore, sST2 was significantly higher in Q4 vs Q1 (1.005; 95% CI=1.001-1.010) and in Q2 (R=0.16; cystatin C, IQR 1.0, and I=0.12; as CRP (R=0.11), and sPLA2 (R=0.16), respectively (all p-values <0.001). During a median follow-up of 10.0 years, 205 patients (19.0%) experienced a fatal- or non-fatal subsequent CVD event. In age and sex adjusted model, sST2 was associated with a hazard ratio (HR) for secondary CVD events of 1.51 (95% CI 1.03-2.22) when extreme quartiles (Q4 vs Q1) were compared. However, further adjustment for clinical factors attenuated the association (HR 1.39; 95% CI 0.94-2.06). By contrast, a statistically significant association was still seen with total mortality (N=173 deaths) in multivariable analyses comparing Q4 vs Q1 with a HR of 1.71 (95% CI 1.002-1.14); p=0.008] were the variables which remained associated with mortality. Levels of sST2 were also significantly associated with the risk of mortality even after adjusting for the CHADS2–VASc score [HR 1.007 (1.001-1.913); p=0.014].

**Conclusions:** Elevated levels of sST2 in stable CHD patients did not independently predict subsequent CVD events but overall mortality in a secondary prevention cohort with long-term follow-up.

**P1285 | BEDSIDE**

A comparison of soluble ST2 and high sensitivity C-reactive protein for prediction of cardiovascular mortality in the Electricity Generating Authority of Thailand cohort study

P. Chanyavich1, J. Januzzi3, P. Vathesatogkit1, O. See1, A. Bayes-Genis2, J. Januzzi3, P. Vathesatogkit1

**Background:** Soluble ST2 (sST2) is increased by cardiomyocyte stretch and inflammation. It has been studied in select community-based Western cohorts. This is the first study to evaluate if sST2 is an independent predictor of cardiovascular mortality in the Thai population and how it compares to highly sensitive C-reactive protein (hsCRP) for this application.

**Methods:** Concentrations of sST2 and hsCRP were measured in 2,058 employees of the Electricity Generating Authority of Thailand (EGAT Cohort Study) from sera stored in 2002. Participants’ baseline characteristics were reviewed and covariates identified which were then categorized by quartiles of sST2 and hsCRP concentrations. Association with all-cause mortality, cardiovascular and non-cardiovascular mortality in 2012 was assessed.

**Results:** In 2,058 participants (mean age 59 years, 75.8% male), the median of sST2 was 18.39 ng/ml and the median of hsCRP was 1.47 mg/l. Male sex, prior history of cardiovascular disease, smoking status, fasting plasma glucose, and serum creatinine were associated with higher sST2 levels. The cut-point of sST2 and hsCRP in 4th quartiles were 23 ng/ml and 3.1 mg/l, respectively. There was no correlation between these two markers (Spearman’s ρ=0.007). During the 10-year follow-up, 192 (9.3%) died; 106 participants (5.2%) underwent coronary angiography; and 95 participants (4.6%) required revascularization. sST2 in 4th quartile was associated with increased all-cause mortality (OR=2.75; 95% CI=1.77-4.25; p<.001). Cardiovascular mortality also increased significantly across sST2 categories from 8.3% in the 1st quartile to 44.4% in the 4th quartiles (OR=5.47; 95% CI=1.56-18.90; p<0.01). After adjusted with other cardiovascular risk factors, sST2 >23 ng/mL showed a strong predictor of cardiac death (HR=4.19; 95% CI=1.10-16.90; p=0.04). hsCRP only predicted all-cause mortality (p<0.01).

**Conclusions:** In this worker-based Thai cohort, sST2 strongly predicted cardiovascular mortality, and was superior to hsCRP for this application.

**P1286 | BEDSIDE**

Predictive role of st2 for mortality in anticoagulated patients with atrial fibrillation

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**Background:** Atrial fibrillation (AF) is associated with high morbidity and mortality. For assessing prognosis in AF, clinical risk scores are recommended for initiating oral anticoagulation (OAC) reduces the risk of stroke and death.

ever the risk of total and cardiovascular mortality remains high in this type of patients, even under OAC. It has been observed that rates of mortality, heart failure, myocardial infarction and stroke increase with older age and risk scores. Biomarkers may add significant information regarding mortality. ST2 is a member of the interleukin-1 receptor family. Patient’s risk of mortality and morbidity increases with ST2 levels—30 ng/ml in patients with heart failure or acute coronary syndrome. We assessed the predictive value of ST2 levels in an unselected “real world” cohort of anticoagulated AF patients seen in everyday clinical practice.

**Methods:** We studied 562 patients (49% male; median age 77 [IQR 71-82]) with permanent AF who were stable (for at least 6 months) on OAC (INRs 2.0-3.0). ST2 levels were quantified by a quantitative sandwich monoclonal ELISA. Patients were followed-up for up to 4 years, and adverse events of all cause mortality were recorded. A Cox regression analysis was performed using ST2 levels as a continuous variable.

**Results:** Median (IQR) of ST2 levels were 51.23 (39.09-67.40) ng/mL. Median follow-up was 1587 days [IQR 1482-1617] days, and during this period, 91 patients died (7.32%)/year). The c-statistic for ST2 was 0.58; p=0.033. On multivariate analysis, age [1.09 (1.05-1.13); p<0.001], diabetes mellitus [1.76 (1.08-2.88); p=0.023], previous stroke [2.16 (1.29-3.60); p<0.003], and ST2 levels [1.002 (1.002-1.14); p<0.008] were the variables which remained associated with mortality. Levels of ST2 were also significantly associated with the risk of mortality even after adjusting for the CHA2DS2–VASc score [HR 1.007 (1.001-1.913); p=0.014].

**Conclusions:** ST2 levels may be employed to lower such risks.
iment of heart failure (HF) through insulin resistance and chronic inflammation. Omentin-1 is a novel adipokine and associated with incident coronary artery disease. However, it remains unclear whether serum omentin-1 levels are associated with cardiac prognosis in patients with HF.

Methods: We measured serum omentin-1 levels at admission in 156 consecutive patients with HF and 20 control subjects without signs of significant heart diseases. We prospectively followed patients with HF for the end points of cardiac death or re-hospitalization for worsening HF.

Results: Serum omentin-1 levels were significantly lower in patients with HF compared with control subjects. Furthermore, serum omentin-1 levels were markedly lower in HF patients with cardiac events compared with those without. Serum omentin-1 levels were decreased with advancing New York Heart Association (NYHA) functional class, whereas serum omentin-1 levels did not correlate with serum brain natriuretic peptide levels (r=0.217). Then we divided the patients into 2 groups based on the median serum omentin-1 level. Kaplan-Meier analysis revealed that significantly higher cardiac event rates were observed in low omentin-1 group compared with high omentin-1 group (log-rank test p < 0.001). Cox analysis showed that decreased serum omentin-1 level (hazard ratio 1.76, 95% CI 1.43-3.56) was independently associated with cardiac events after adjustment of predictors that were significant by univariate analysis.

Figure 1. Kaplan Meier analysis

Conclusion: Decreased serum omentin-1 levels were associated with poor cardiac prognosis in patients with HF.

P1289 | BEDSIDE Plasma omentin significantly predicts cardiovascular events independently from the presence and extent of angiographically determined baseline coronary artery disease

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Purpose: No prospective data on the power of the new adipocytokine omentin to predict cardiovascular events are available. We therefore aimed at investigating i) the association of plasma omentin with cardiometabolic risk markers, ii) its association with angiographically determined coronary atherosclerosis, and iii) the power of plasma omentin to predict cardiovascular events.

Methods: We measured plasma omentin in a series of 295 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; presence of baseline CAD was defined as the presence of any lumen irregularities at angiography; the extent of baseline CAD was defined as the number of significant coronary stenoses ≥50%; prospectively cardiovascular events were recorded over a mean follow-up period of 3.5 years.

Results: During this period, 17.6% of our patients suffered cardiovascular events, corresponding to an annual event rate of 5.3%. Plasma omentin did not differ significantly between patients with and subjects without significant CAD (p=0.783), but prospectively omentin significantly predicted cardiovascular events after adjustment for age, gender, BMI, diabetes, hypertension, HDL cholesterol, HDL cholesterol and smoking with a standardized adjusted hazard ratio (HR) of 1.41 (95% CI 1.16-1.72), p=0.001, as well as after additional adjustment for the presence and extent of CAD at the baseline angiography (HR 1.52 [95%CI 1.23-1.86]), p=0.001.

Conclusions: From this first prospective evaluation of the cardiovascular risk associated with plasma omentin we conclude that elevated omentin is a strong predictor of cardiovascular events independently from the presence of baseline CAD.

P1290 | BEDSIDE Combining NT-pro-BNP with a novel restitution based biomarker substantially improves prediction of sudden cardiac death risk

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Purpose: The Regional Restitution Instability Index (R2I2) is a promising new ECG based biomarker of sudden cardiac death (SCD). This abstract explores the potential of a combined R2I2 and NT-pro-BNP SCD risk marker in an ischaemic cardiomyopathy cohort.

Methods: Blinded prospective observational study. Study group: 55 ischaemic cardiomyopathy patients undergoing risk stratification for implantable cardioverter defibrillator (ICD). The R2I2 technique has been described previously: an EP study is performed and ECG surrogates for action potential duration and diastolic interval are used to measure restitution heterogeneity. Plasma samples obtained on the day of the ICD procedure were assayed for NT-pro-BNP.

Results: During median follow up of 22 months, 15 patients experienced ventricular arrhythmia (VA)/SCD. R2I2 was significantly higher in patients experiencing VA/SCD than those not (mean±SEM: 1.12±0.05 vs 0.84±0.09, p=0.004). R2I2 was independent of log NT-pro-BNP and left ventricular ejection fraction in prediction of endpoint (Cox model, p=0.001). Partioning patients using a log NT-pro-BNP≥2.65 gave a significantly higher rate of VA/SCD in those with high versus low log NT-pro-BNP (38% vs. 6%, p=0.01). Patients with R2I2≥1.03 and log NT-pro-BNP≥2.65 had a hazard ratio for VA/SCD 17 times that of patients negative for both (Cox model, p=0.007). Kaplan Meier analysis (Figure 1) showed significant separation in rates of VA/SCD in patients stratified by R2I2≥1.03 and log NT-pro-BNP≥2.65 (log-rank, p<0.0001).

Conclusion: Combined R2I2+NT-pro-BNP identify patients with particularly high risk of ventricular arrhythmia/SCD. These patients might benefit from careful treatment optimisation. R2I2+NT-pro-BNP might retain sufficient positive predictive value for application to lower risk cohorts.

P1291 | SPOTLIGHT SDMA and L-arginine correlate with subclinical atherosclerosis in a large population cohort

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Circulating levels of arginine derivatives can predict cardiovascular mortality. However, their role as atherosclerotic biomarkers is unclear. Asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) may contribute to subclinical atherosclerosis by inhibition of endothelial nitric oxide (NO) synthase and cellular L-argnine (ARG) uptake, respectively. ARG up-regulates endothelial NO production and thus maybe atheroprotective. Therefore, we tested if ADMA, SDMA, and the sum of both (DMA) are positively, while ARG is inversely correlated with carotid inter-media thickness (IMT) and presence of atherosclerotic plaque. Cross-sectional data of 2007 subjects (48.2% o, age: 45 – 81 years) from the Study of Health in Pomerania (SHIP-0) was used. All adjusted models were corrected for sex, age, smoking status, waist-to-hip ratio and glomerular filtration rate. An adjusted ANOVA was fitted to ADMA, SDMA, DMA, and ARG plasma concentration tertiles with continuous log-corrected IMT. Associations between plasma arginine derivative concentrations and increased IMT, defined as above the 75th sex- and age-specific quartile, as well as the presence of atherosclerotic plaque were calculated using logistic regression models. Increased IMT was found in 517 subjects (25.7%). SDMA plasma concentration tertiles were significantly associated with IMT, while ADMA, DMA, and ARG were not. Post-hoc analysis identified a positive correlation and significant differences between medium and high plasma SDMA concentrations [-33rd: 0.816 (0.789; 0.845), 33rd–66th: 0.778 (0.755; 0.802), >66th: 0.824 (0.796; 0.853)]. High SDMA and DMA concentrations were related to higher odds of increased IMT in the adjusted [SDMA OR 1.371; 95% CI (1.068; 1.760) and DMA OR 1.310 (1.024; 1.676)] and unadjusted model. A total of 1413 subjects (70.4%) had carotid atherosclerotic plaques. Non-adjusted logistic regression models identified a significant positive association for the presence of atherosclerotic plaque with ADMA, SDMA, and ARG. After adjustment only ARG remained significant, demonstrating increased odds for atherosclerotic plaques with high ARG concentrations in the non-adjusted and adjusted model [OR 1.367; 95% CI (1.040; 1.798)].

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atherosclerosis. Therefore, whether arginine derivatives may serve as atherosclerotic biomarkers deserves further research.

P1292 | BEDSIDE
Impact of indoxyl sulfate on coronary plaques in patients on hemodialysis; IS-HD study
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Background: Chronic kidney disease (CKD) is an independent risk factor for cardiovascular disease (CVD). Indoxyl sulfate (IS) is a uremic toxin (UT) that is associated with CVD and mortality in CKD patients. However, an impact of serum IS level on coronary plaque burden (CPB) or coronary artery calcium (CAC) is unknown. Therefore, the aim of this study is to investigate the relationship between serum IS level and CPB or CAC in patients on hemodialysis.

Methods and results: The study is prospective observational study and registered with university hospital medical information network (UMIN) clinical trial registration: UMIN000009500. We enrolled 30 patients (19 men, 67.4±10.7 years) on hemodialysis who underwent coronary computed tomographic angiography (CCTA) with 320-rows (Aquilion One) for suspected CVD between December 2012 and November 2013. The patients with prior coronary artery bypass grafting, prior pacemaker implantation, and severe heart failure (New York Heart Association Classification III - IV) were excluded. CCTA with 320-rows was performed on a dialysis-free day and blood samples were collected on the same morning before CCTA. Serum IS level and various oxidative and inflammatory markers, such as carboxylated advanced glycation end products (CAGE), C-reactive protein (CRP), and tumor necrosis factor-β (TNF-β) were measured. Nonenhanced scans were used to evaluate the total amount of CAC according to the Agatston approach. The plaque quantification was performed using dedicated quantitative software with a 3D registration algorithm (QAngio CT 2.0.5, Medis medical imaging systems, Leiden, the Netherlands). By univariate analysis, CPB was significantly correlated with serum IS level (r=0.533, p<0.002). Good correlation for CAC were observed for HbA1c (r=0.403, p=0.027), serum potassium (r=0.429, p=0.020), right carotid artery intima-media thickness (r=0.386, p=0.039), and serum ICAM-1 (r = −0.366, p=0.047). Furthermore, CPB was significantly higher in patients with hyperuricemia (p<0.014), and CAC was significantly higher in patients with vitamin D preparation (p=0.004). Multivariate analysis identified serum IS level and hyperuricemia as predictive factors of greater CPB after controlling for the above-mentioned variables. In contrast, no significant predictive factors were identified for CAC.

Conclusions: We are able to correlate, for the first time, serum IS level and CPB in patients on hemodialysis. Our findings provide a critically important link between UT and atherogenic CVD in hemodialysis patients.

P1293 | BENCH
Profiling of circulating microRNAs in interventional cardiology patients occupationally exposed to chronic ionizing radiation
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Background: Aberrant expression of circulating microRNA (miRNA) is related to various diseases, including cancers and cardiovascular disease. However, it is unknown whether dysregulation of miRNAs may occur following exposure to chronic ionizing radiation exposure. Aim of this study was to investigate the plasma miRNA profile in interventional cardiologists working in cath laboratory.

Methods: Global miRNA expression was performed in 10 interventional male cardiologists (age = 54.5±4 years) and 10 healthy subjects (age = 53.2±5.5 years). RNA was isolated from plasma using the miRNeasy Kit (QIagen) and hybridized on Agilent MicroRNA 60K array containing probes for 2006 human miRNAs. Highly deregulated miRNAs were validated using qRT-PCR. Target genes and biological pathways were determined with DAVID (http://david.abcc.ncifcrf.gov) and the interactions were visualized with Cytoscape (http://cytoscape.org).

Results: Microarray analysis revealed a significant decrease of hsa-miR-134 (p=0.00045), hsa-miR-575 (p=0.0023), hsa-miR-1275 (p=0.00027) and hsa-miR-2392 (p=0.0011) in exposed when compared to controls. The relative fold changes of the qRT-PCR validation were in line with the microarray data. Bioinformatic analysis revealed 928 predicted target genes, most of which are involved in DNA repair, apoptosis, neuronal brain function, control of spermatogenesis and metabolic process (figure). Deregulated miRNAs were also previously reported for potential biomarkers of disease (cancer and neuropsychiatric disorders), suggesting the possibility that radiation exposure might interfere with the health risk.

Conclusion: These findings showed dysregulation of specific miRNA profiles, giving clues for better understanding the health risk from exposure to low dose ionizing radiation.

P1294 | BEDSIDE
Circulating miRNA and the severity of coronary artery disease
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Background: The individual risk of a patient with coronary artery disease (CAD) for developing an acute coronary syndrome (ACS) is currently difficult to estimate. To date, there is no specific marker able to predict the risk for ACS.

Objectives: We aimed to identify such a biomarker by studying the distribution of miRNA in 4 groups of patients: SA (stable angina, n=22), UA (unstable angina, n=21), MI1 (patients 1 month after myocardial infarction, n=11), RF (subjects with CAD risk factors, but no significant CAD, n=10), compared to C (healthy subjects, n=10).

Methods: miRNA were isolated from pooled sera of SA, UA, MI1, RF and individuals following, a screening for 84 miRNA was performed. Fold change (FC) values of analyzed miRNA were expressed relative to C group. MiR-125a, miR-146a, miR-33a were validated using qRT-PCR. Target genes and biological pathways were determined with DAVID (http://david.abcc.ncifcrf.gov).

Results: Screening analysis showed that miR-122a (FC 63.07), miR-486a (FC 52.89), miR-92a (FC 51.19) had the highest values compared to C. All miRNA had higher serum levels in SA, UA, RF, MI1 groups, compared to C (p<0.05 for all). MiR-486a and miR-92a had higher levels in patients with MI1 than UA. MiR-125a, miR-146a, and miR-33a did not differ between groups.

Conclusions: In the analysed cohort the selected miRNA failed to discriminate between SA and UA. However, in more severe forms of CAD (ie MI1), levels of miR-486a and miR-92a were increased compared to UA.

GENDER, FAMILY AND CARDIOVASCULAR RISK

P1295 | SPOTLIGHT
Sex differences in the prognostic impact of left ventricular hypertrophy in members of a cohort with high prevalence of obesity and diabetes: the Strong Heart Study
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Purpose: In the Strong Heart Study (SHS) cohort, women exhibit higher left ventricular (LV) mass index (LVMi) than men, a characteristic associated with central adiposity. There is no information on whether LV hypertrophy (LVH)-associated outcome is different in men and women, in relation to adiposity.

Conclusions: The examined cohort the selected miRNA failed to discriminate between SA and UA. However, in more severe forms of CAD (ie MI1), levels of miR-486a and miR-92a were increased compared to UA.
Conclusions: a significantly stronger predictor of cardiovascular events among women than men. HbA1c again was statistically significant (p=0.011), indicating that HbA1c was justed OR for a 1% increase in HbA1c (HR 2.08 [1.24-3.03]; p<0.001), the difference between men and women was proven to be statistically significant by sex-LVH interaction term (HR=1.21, [1.07-1.37], p<0.002). In women, the effect of LVH was independent of significant association with age (HR=1.02/year, [1.00-1.04]), PP (PP=1.02/mmHg, [1.01-1.02]), diabetes (HR=2.53, [1.95-3.30]), smoking (HR=1.49, [1.13-1.96]), HDL-cholesterol (HR=0.99/mg Dl, [0.98-1.00]), and concentric LV geometry (HR=1.84, [1.92-2.84], all p<0.05), without significant impact for anthropometrics. When, excess of LV mass was added to the previous model, observed/predicted LVH was significantly associated with CV outcome in women (HR=1.42 [95% CI 1.09-1.84], p=0.009) than in men (HR=1.25 [0.86-1.83]), gender difference between men and women was statistically significant by p<0.001), but not in hypertensive (41 vs. 43%). During follow-up, 651 LV events occurred. After adjusting for confounders, LVH increased CV risk quantitatively more in women (HR=1.10/10% [1.01-1.17], p=0.02) but not in men (HR=1.00/10%, [0.90-1.10]).

Results: Compared to men, women had higher prevalences of obesity (58 vs. 45%), diabetes (48 vs. 40%), LVH (23 vs. 14%, all p<0.001), but not of hypertensive (41 vs. 43%). During follow-up, 651 LV events occurred. After adjusting for confounders, LVH increased CV risk quantitatively more in women (HR=1.10/10% [1.01-1.17], p=0.02) but not in men (HR=1.00/10%, [0.90-1.10]).

Conclusions: In a population with high prevalence of obesity and diabetes, adjusting for potential confounders including central adiposity, LVH and excess of LVH were associated with higher risk of CV events in women than in men.

Methods: We studied 2520 participants to 2nd SHS exam, free of prevalent cardiovascular (CV) disease (59.8 years, 64% women, 54% obese, 45% diabetic). LVH was assessed by echocardiographic LVM, using SHS-specific cut-off point, maximizing the population risk attributable to LVH (≥47.2 g/m²), and excess of LVH (by ratio of observed LVH to the value predicted by sex, stroke work and height). The association of LVH with incident CV events (combined fatal and non-fatal heart failure, coronary artery and cerebrovascular disease) was evaluated by use-specific Cox models (median follow-up=14 yrs), adjusting for variables that were significantly different between men and women: age, pulse pressure (PP), waist/hip ratio, adipose body mass (by bioelectric impedance), diabetes, smoking status, HDL cholesterol and concentric LV geometry (relative wall thickness ≥0.43). Attention was paid to avoid substantial multicollinearity among covariates (variance inflation factor <2).

Results: Compared to men, women had higher prevalences of obesity (58 vs. 45%), diabetes (48 vs. 40%), LVH (23 vs. 14%, all p<0.001), but not of hypertension (41 vs. 43%). During follow-up, 651 LV events occurred. After adjusting for confounders, LVH increased CV risk quantitatively more in women (HR=1.10/10% [1.01-1.17], p=0.02) but not in men (HR=1.00/10%, [0.90-1.10]).

Conclusions: In a population with high prevalence of obesity and diabetes, adjusting for potential confounders including central adiposity, LVH and excess of LVH were associated with higher risk of CV events in women than in men.
P1301 | BEDSIDE
Impact of gender, co-morbidity and social factors on labour market affiliation after first admission for acute coronary syndrome
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Background: Over the last decades survival after acute coronary syndrome (ACS) has improved, leading to an increasing number of patients returning to work, but little is known about factors that may influence their labour market affiliation. This study examines the impact of gender, co-morbidity and socio-economic position on subsequent labour market affiliation in patients admitted for the first time with ACS.

Methods: From 2001 to 2009 all first-time hospitalisations for ACS were identified in the Danish National Patient Registry (n=79,714). Data on sick leave, unemployment and retirement were obtained from a national register covering all citizens. The 21,926 patients, aged 18–63 years, who had survived 30 days and were part of the workforce at the time of diagnosis were included in the analyses where subsequent transition between the above labour market states was examined using Cox proportional hazards models.

Findings: A total of 37% of patients were in work 30 days after first ACS diagnosis, while 55% were on sick leave and 8% were unemployed. Table 1 shows that the proportion in work increased, while the proportion on sick leave decreased during follow-up. Seventy-nine per cent returned to work once during follow-up. This probability was highest among males, those below 50 years, living with a partner, the highest educated, with higher occupations, having NSTEMI or percutaneous coronary intervention and with no co-morbidity. During five years follow-up, 43% retired due to disability or voluntary early pension. Female gender, low education, basic occupation, co-morbidity and having an invasive procedure and receiving sickness benefits or being unemployed 30 days after admission were associated with increased probability of early retirement.

Table 1. Workforce participation

<table>
<thead>
<tr>
<th>Time after diagnosis</th>
<th>N (%)</th>
<th>N (%)</th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td>Part of the workforce 21926 (100)</td>
<td>21869 (99.7)</td>
<td>19664 (98.4)</td>
<td>15468 (88.0)</td>
</tr>
<tr>
<td></td>
<td>In work 8150 (37.2)</td>
<td>8777 (40.1)</td>
<td>8856 (45.0)</td>
<td>10,079 (55.2)</td>
</tr>
<tr>
<td></td>
<td>Unemployed 1743 (8.0)</td>
<td>1850 (8.5)</td>
<td>1936 (9.9)</td>
<td>2878 (15.2)</td>
</tr>
<tr>
<td></td>
<td>Sick leave 12033 (54.9)</td>
<td>11220 (51.4)</td>
<td>8852 (45.0)</td>
<td>2511 (13.2)</td>
</tr>
</tbody>
</table>

Conclusion: About half of patients with first-time ACS are in work shortly after the event. Women, the socially disadvantaged, those with presumed severe events and co-morbidity have lower rates of return.
yzed. These users self-reported demographic (including age, gender and self-reported family history of CVD) and classic CVD risk factor information (blood pressure, diabetes, total and HDL cholesterol, BMI, smoking). Based on these data, an individual’s estimated 10 year CVD-risk was calculated according Framingham CVD risk models and translated into a Heart Age. Subjects included in the analyses were free from CVD, aged between 21 and 80 years and self-reported information on CVD risk factors, fruit and vegetable consumption, physical activity, weight and waist circumference.

**Results:** 39% of users reported a family history of CVD in at least one parent and 13% of users reported a family history of premature CVD (father younger than 55 years of age; mother younger than 65 years of age). Heart age scores were higher in those with a family history of CVD (+5.8 years vs. real age) than those without (+4.3 years vs. real age) and this was more marked in those reporting two parents with CVD (+6.9 years vs. real age). Those users reporting a family history were more likely to report a known cholesterol level (39%-48%) than those without a family history (27%). They were also more likely to report a known blood pressure value (65%-70%) than those without (56%). On the other hand minimal differences existed in lifestyle behaviours between those reporting a family history of CVD and no family history.

**Conclusions:** These analyses suggest that those with a family history of CVD had higher heart ages than those who did not. Nevertheless, whilst awareness of cholesterol and blood pressure levels were greater in those with a family history of CVD, adherence to lifestyle modification was not different between the two groups. This suggests that raising awareness of family history alone is unlikely to be sufficient to lead to lifestyle changes.

**P1305 | BEDSIDE**

**Spousal concordance for cardiovascular health in a primary care based sample**


**Purpose:** Previous research has demonstrated spousal concordance for cardiovascular (CV) risk factors. However, there is a dearth of research on overall CV health among couples. The American Heart Association devised definitions for poor, intermediate and ideal CV health based on 7 health metrics; smoking, BMI, physical activity, diet, blood pressure, cholesterol and glucose. Our aim was to examine these metrics and concordance levels for CV health among couples from a community based sample and to examine if the CV health status of an individual is associated with that of their spouse.

**Methods:** The Mitchelstown Study was established to examine CV risk factors in adults with CVD and diabetes in a middle-aged Irish sample. For the present study, potential couples were identified as 2 study participants living at the same address with the same telephone number. This list was cross-referenced with reported marital status by questionnaire and the electronic patient record. Information on the individual CV health metrics were collected in health standardised methods. All participants were categorised into ideal, intermediate and poor categories for each of the individual metrics and for overall CV health. The prevalence of each category was calculated. The 0-7 point and 0-14 point CV health metrics scores were computed and compared in same sex and opposite sex couples using linear regression.

**Results:** Of 2047 participants, 191 potential couples were identified. We excluded 6 sibling pairs, 1 divorced couple and 3 other couples who did not report being married in the baseline questionnaire. Analysis was carried out on 181 couples. The mean age of participants was 61 years (SD 8 years); 50% were women. There was significant association between husbands and wives for smoking status (p < 0.05), diet (p < 0.05), blood pressure (p < 0.05), total cholesterol (p < 0.05) and glucose (p < 0.05). No couple had ideal CV health (i.e. both spouses with 7 ideal health metrics). The majority of couples (n=127, 69%) were concordant for poor CV health. There was a significant relationship between spouses for both CV health metrics scores (p < 0.05).

**Conclusion:** The majority of couples had poor CV health. Our results suggest that an individual’s overall CV health status is associated with that of their spouse. Therefore interventions targeting couples and families offer an opportunity to optimise the effect of preventative strategies. The CV health metric system could also potentially be used as a way of communicating CV risk status to couples as a strategy to promote lifestyle modification.

**NOVEL BIOMARKERS PART II**

**P1307 | BEDSIDE**

**Growth differentiation factor 15 is independently associated with cardiovascular events and total mortality in patients with stable coronary heart disease: 10-year follow-up of the KAROLA Study**

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**Purpose:** Growth differentiation factor 15 (GDF-15) belongs to the transforming growth factor β superfamily and is involved in inflammatory and apoptotic pathways. It has been proposed as a predictor of mortality and disease progression in patients with cardiovascular (CV) disease. We evaluated if baseline GDF-15 levels were associated with subsequent CV events and total mortality in patients with stable coronary heart disease.

**Methods:** GDF-15 serum concentrations were measured at baseline in 1073 subjects aged 30-70 years participating in an in-patient cardiac rehabilitation program (median follow-up 10 years). Cox-proportional hazard models were used to evaluate the association of log-transformed (in GDF-15 baseline levels as a continu- ous variable and by quartiles) with subsequent CV events (myocardial infarction, stroke, cardiovascular death) and total mortality adjusting for age, sex, body mass index, left ventricular function, smoking, total and HDL-Cholesterol, renal function, diabetes, hypertension, CHD risk classification, adherence to lifestyle and using Cox regression models with time-dependent variables.

**Results:** In our study sample (84.3% men, mean age 59 years) there were a total of 172 CV events and 152 deaths. The median GDF-15 levels were 1233.0 pg/mL (IQR 917.0, 1703.0) at baseline. A one unit increment of ln GDF-15 was associated with a hazard ratio (HR) of 2.19 [95% CI 1.67, 2.87] for a subsequent CV event, and with a HR of 2.65 [95% CI 2.03, 3.47] for death adjusting for age and sex. Comparing extreme quartiles, patients in the top quartile had a HR of 2.62 for a CV event [95% CI 1.60, 4.28] after adjustment for age and sex. In multivariable analysis this association was attenuated and non-significant. However, the trend test showed a p-value=0.028 with the following hazard ratios: 2nd quartile 0.84 [95% CI 0.49, 1.44], 3rd quartile 1.06 [95% CI 0.62, 1.82], and 4th quartile 1.59 [95% CI 0.99, 2.53], (p=0.01, 2.71). Using total mortality as an endpoint, a multivariable analysis a HR of 5.28 [95% CI 2.72, 10.24] was seen for those in the top quartile. After further adjustment this association remained statistically significant with a HR of 2.85 [95% CI 1.42, 5.70].

**Conclusions:** Baseline levels of GDF-15 measured after an acute event were associated with subsequent CV events as well as 10-year total mortality in patients with stable coronary heart disease.
P1310 | BEDSIDE

The association between resistin concentrations and the occurrence of cardiovascular disease in older persons: the health, aging and body composition (Health ABC) study


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Background: An association between resistin and cardiovascular disease has been observed in several studies. However, information on the association of resistin concentrations with cardiovascular outcomes in older adults is limited. Thus, the aim of this study was to assess the association of resistin concentrations with cardiovascular events in older adults.

Methods: Participants were selected from baseline examinations of 5,886 participants aged 70–79 years in the Health ABC study. Resulin concentrations were assessed in whole blood. Cardiovascular events were determined by adjudication from medical records as of December 31, 2014. Cox proportional hazards regression was used for analysis.

Results: During a median follow-up of 11.5 years, 884 participants developed CHD events (559 “hard” events), 333 stroke events and 1106 CVD events; all of these events were associated with resistin concentrations. In clinical variables adjusted model, HsR of resistin (highest -24.31 ng/mL vs. lowest quartile-14.01 ng/mL) were associated with CHD events (P=0.002 for trend) and total CVD events (P=0.003 for trend). After adjusting for smoking, race, total and HDL-cholesterol, triglycerides, fasting glucose, systolic blood pressure, smoking, body mass index, creatinine, and history of CVD, diabetes, and hypertension. We further adjusted for biomarkers of inflammation and insulin resistance (HbA1c, insulin, leptin, adiponectin, C reactive protein, interleukin-6 and tumor necrosis factors-α).

Conclusion: Resistin is implicated in promoting insulin resistance and inflammation. Prospective data regarding the association between resistin levels and cardiovascular outcomes in CHD and CVD events independently of clinical variables. The association is partially independent with biomarkers of insulin resistance and inflammation.

P1311 | BEDSIDE

Urinary proteomics for the identification of disease-specific biomarkers in heart failure with reduced ejection fraction

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Background: Myocardial and extracellular matrix remodeling is a cardinal feature of heart failure with reduced ejection fraction (HFrEF). Biomarkers for the detection of HFrEF are of great clinical importance.

Methods: We selected three postulates on 13,224 Scottich Heart Health Extended Cohort (SHHEC) participants followed 22 years, using archived serum samples for biomarker analysis.

Results: We first demonstrated that serum levels of sFlt-1 were significantly increased in patients with HFrEF, compared to controls. An increased sFlt-1 value may serve as a predictor of cardiovascular events in CKD.

Conclusion: Urinary proteomic analysis was able to identify a set of HFrEF-specific urine peptides that may serve as potential biomarkers of the syndrome. Most of the identified peptides were associated with extracellular matrix remodelling.
vized to grade the complexity of coronary artery disease (CAD). The SYNTAX score was able to stratify risk for very long-term adverse clinical outcomes. However, the relationships of these two markers with the complexity and severity of CAD assessed with the SYNTAX score are unknown.

**Method and results:** We enrolled a total of 387 consecutive patients who electively underwent coronary artery angiography (CAG). Pre-procedural serum levels of high-sensitivity C-reactive protein (hsCRP), SAA-LDL, and AT-LDL were measured by specific enzyme-linked immunosorbent assays. The SYNTAX score was calculated according to CAG results. The mean age was 70.11 (SD years), and the rate male gender was 61%. The prevalence of hypertension, diabetes, dyslipidemia, and a history of smoking habit were 80.45, 63, and 60%, respectively. Patients were divided into 2 groups according to the SYNTAX score: those with low- (<22, n=333) and intermediate/high-risk group (≥22, n=24) there were. There was no significant difference in age, ratio of male gender, body mass index, lipid and metabolic profiles, and the prevalence of hypertension, dyslipidemia, diabetes, and history of smoking habit among the two groups. However, serum levels of AT-LDL (P=0.012), but not hsCRP (P=0.4) or SAA-LDL (P=0.11), were significantly higher in the intermediate/high-risk group, even after adjusting for established risk factors (OR, 1.6; 95% CI, 1.1-2.4 for 1-SD increase; P=0.015).

**Conclusion:** In simple regression analyses, there was significant positive correlation of AT-LDL (P=0.004), but not hsCRP and SAA-LDL with the SYNTAX score. Stepwise regression analysis, including data on age, a male gender, systolic blood pressure, LDL-cholesterol, HDL-cholesterol, diabetes, history of smoking, hsCRP, SAA-LDL, and AT-LDL (P=0.004), but not hsCRP SAA-LDL, was an independent predictor of the SYNTAX score. Finally, we performed multivariate logistic regression analysis for the intermediate/high-risk group. The AT-LDL level was significantly associated with intermediate/high-risk group, even after adjusting for established risk factors.

**Conclusions:** Our study showed that MTHFR1298 CC and ADAMTS 7 AA increase the risk of late cardiovascular mortality. Since these genes are linked to the endothelial dysfunction and inflammatory cellular processes, carriers of these 2 variants should have a particularly careful secondary prevention, which may justify a search for new therapeutic approaches.

**BIOMARKERS: TROPONIN AND MORE**

**P1317 | BEDSIDE**

Cardiac specific biomarkers and LVH identify differential risk of new-onset reduced versus preserved ejection fraction heart failure in older adults

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**Purpose:** To determine whether biomarkers of subclinical myocardial injury (high sensitive [hs] cTnT) and stress (NT-proBNP) differentiate risk of HFpEF vs. HFrEF among older asymptomatic adults with LVH.

**Methods:** NT-proBNP and hs cTnT were measured in older adults without HF or prior MI in the Cardiovascular Health Study. LVH was determined by echo. HF events were adjudicated over a median 13.1 years as HFpEF (EF<45%) or HFrEF. The risk of each HF type by LVH and age-/sex-stratified tertiles of each biomarker was adjusted for demographics, CV risk factors, and LV relative wall thickness.

**Results:** Among 2347 participants there were 643 incident HF events (215 [33.4%] HFpEF, 150 [23.3%] HFrEF, and 278 [43%] without documented EF). Risk of HFpEF was 5-fold (NT-proBNP) and 7.8-fold (hs cTnT) greater among those with LVH and the highest biomarker tertile vs. those without LVH and lowest biomarkers (Table 1). In contrast, these groups had 3.1-fold and 2.6-fold greater risks of HFpEF (Table 1). There was an interaction (p<0.02) between LVH and NT-proBNP for risk of HFrEF but not HFpEF.

**Table 1**

<table>
<thead>
<tr>
<th>LVH by echo</th>
<th>Tertile of NT-proBNP</th>
<th>Heart failure reduced EF</th>
<th>Heart failure preserved EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>None (n=2053)</td>
<td>1</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes (n=294)</td>
<td>1</td>
<td>1.0 (0.6, 1.7)</td>
<td>1.0 (0.6, 1.6)</td>
</tr>
<tr>
<td>2</td>
<td>1.7 (1.1, 2.2)</td>
<td>1.7 (1.1, 2.6)</td>
<td>1.7 (1.1, 2.3)</td>
</tr>
<tr>
<td>3</td>
<td>2.2 (1.6, 3.7)</td>
<td>2.2 (1.6, 3.7)</td>
<td>2.2 (1.6, 3.7)</td>
</tr>
<tr>
<td>4</td>
<td>2.9 (2.4, 3.6)</td>
<td>2.9 (2.4, 3.6)</td>
<td>2.9 (2.4, 3.6)</td>
</tr>
<tr>
<td>5</td>
<td>3.7 (3.8, 4.9)</td>
<td>3.7 (3.8, 4.9)</td>
<td>3.7 (3.8, 4.9)</td>
</tr>
<tr>
<td>6</td>
<td>4.8 (4.1, 5.5)</td>
<td>4.8 (4.1, 5.5)</td>
<td>4.8 (4.1, 5.5)</td>
</tr>
</tbody>
</table>

**Conclusion:** Cardiac specific biomarkers and LVH identify differential risk of new-onset reduced versus preserved ejection fraction heart failure in older adults.

**BIOMARKERS: TROPONIN AND MORE**

**P1314 | BEDSIDE**

Thyroid-stimulating hormone and premature atrial contractions in a young population

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**Purpose:** Thyroid disorders increase the risk for atrial fibrillation. However, the underlying mechanism of this association remains poorly understood. We therefore assessed the relationship between levels of thyroid-stimulating hormone (TSH) and frequency of premature atrial contractions (PACs).

**Method:** A population-based cohort of healthy adults without prevalent cardiovascular disease, diabetes or body mass index >35kg/m2 aged 25-41 years was included. The number of PACs per participant was obtained from 24-hour electrocardiography (ECG) devices. TSH was quantified from fasting venous blood samples. Multivariable negative binomial regression models were used to assess the relationship between TSH levels and the number of PACs.

**Results:** 2049 participants (median age 37 years) were included in this analysis, of which 46.9% were men. The median TSH (interquartile range (IQR)) was 0.8 (0.4-0.29). Results of the multivariable regression analysis are shown in the table. Risk ratios for the relationship between PAC count and TSH levels were lowest in quartile 2 and 3, assuming a U-shaped association. Both subclinical hypothyroidism (risk ratio (95% confidence interval (95%CI)) 1.88 (1.38, 2.56), p<0.0001) and subclinical hyperthyroidism (risk ratio (95%CI)) 1.82 (1.26, 2.56), p=0.002) were independently associated with PAC count.

**Data for risk ratios.** Fully adjusted model was adjusted for sex, age, body mass index, current smoking, hypertension, high- and low density lipoprotein, creatinine, high-sensitivity C-reactive protein, haemoglobin A1c, physical activity and alcohol consumption.

**Thyroid-stimulating hormone and PACCount**

<table>
<thead>
<tr>
<th>Quartile 1 (n=519)</th>
<th>Quartile 2 (n=515)</th>
<th>Quartile 3 (n=506)</th>
<th>Quartile 4 (n=509)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex/age adjusted</td>
<td>Reference</td>
<td>0.54 (0.43, 0.67)</td>
<td>0.54 (0.43, 0.67)</td>
</tr>
<tr>
<td>Fully adjusted</td>
<td>Reference</td>
<td>0.61 (0.40-0.97)</td>
<td>0.76 (0.58, 0.97)</td>
</tr>
</tbody>
</table>

| Data for risk ratios. | Reference | 1.00 (0.10, 10.00) | 1.00 (0.10, 10.00) | 1.00 (0.10, 10.00) |

**Conclusion:** A U-shaped relationship between TSH level and PAC count was seen in our young and healthy study population, suggesting that both hypo- and hyperthyroidism are related to the frequency of PAC occurrence.
Conclusion: Older adults with elevated hs cTnT or NT-proBNP and LVH are at markedly greater risk for incident HF, especially HFpEF.

P1318 | BEDSIDE
Quantification of troponin shows worse discriminatory capacity in the prediction of both large infarct size and poor left ventricular ejection fraction in the presence of ventricular hypertrophy
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Introduction and purpose: Infarct size estimation using biomarkers - creatine kinase (CK) and troponin (cTn) - is currently being evaluated as endpoint in many clinical trials. We recently described for the first time in a retrospective study that peak of cTn could overestimate infarct size in presence of left ventricular hypertrophy (LVH). Prospective evidence regarding this hypothesis is needed and focuses the purpose of the present work.

Methods: A cohort of 140 patients with anterior ST-segment elevation acute myocardial infarction was prospectively recruited. A full cardiac magnetic resonance (CMR) study was performed 5-7 days after myocardial infarction, and CK and cTn systemic values were serially measured. The cohort was categorized in tertils according to indexed LV mass in CMR. Analysis of ROC curves were performed to study the discriminatory capacity of AUC of Tn vs. AUC of CK in predicting LVEF less than 40% and infarct size greater than 25%, in the lower vs. upper tertil.

Results: Discriminatory capacity of AUC of Tn in predicting poor LVEF and large infarct size was significantly worse for the upper tertil vs. lower tertil of indexed LV mass: 0.7146 vs. 0.9261 (p=0.02, Figure A) and 0.7903 vs. 0.9330 (p=0.05, Figure B), respectively. No significant differences were found regarding discriminatory capacity of AUC of CK for neither of the studied parameters.

Conclusions: Quantification of released cardiac troponin offers lower discriminatory capacity in the prediction of both large infarct size and poor left ventricular ejection fraction in the presence of ventricular hypertrophy. Left ventricular hypertrophy should be taken into consideration when infarct size and ejection fraction is estimated or predicted by troponin release.

P1319 | BEDSIDE
High-sensitivity troponin t and troponin i in the prediction of subsequent cardiovascular disease events in stable coronary heart disease patients: 10-year follow-up of a baseline study
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Purpose: There is increasing evidence that even slightly elevated circulating troponin levels in patients with stable coronary heart disease (CHD) several weeks after an acute event are associated with adverse outcome. Since initial studies have indicated that there may be differences between troponins concerning their kinetics and other properties, we assessed the predictive value of two new high-sensitivity (hs) troponin assays for subsequent cardiovascular disease (CVD) events in stable CHD patients, simultaneously controlling for a large number of potential confounders.

Methods: Plasma concentrations of hsTnT (Roche Elecsys) and hsTnI (Abbott ARCHITECT) were measured at baseline and in a cohort of 1,039 patients aged 35-70 years with CHD. A Cox proportional hazards model was used to determine the prognostic value of hsTnT compared to hsTnI on a combined CVD endpoint (cardiac death, non-fatal MI and stroke) after adjustment for established risk factors (i.e., age, gender, school duration, smoking habits, number of affected vessels, initial management of CHD, HDL- and LDL-cholesterol) and additionally, for other emerging biomarkers.

Results: Median levels of hsTnT and hsTnI were 14.1 ng/L (IQR 9.1-22.2) and 14.0 ng/L (IQR 6.6-24.2), respectively, with all values above the level of detection. The age and gender adjusted Spearman partial correlation coefficient between both troponins was 0.66 (p<0.0001). Levels of both troponins were associated with higher age, body mass index, a higher number of affected vessels, and decreased left-ventricular function. During a median follow-up of 10 years, 200 patients (19.2%) experienced an adverse CVD event. In a multivariate model adjusted for established risk factors and including both troponins, hsTnT was associated with a hazard ratio (HR) of subsequent CVD events of 2.21 (95% CI, 1.19-4.59) when extreme quartiles were compared. The respective HR for hs TnI was 2.09 (95% CI, 1.11-3.82). However, further adjustment for NT-proBNP and GDF-15 attenuated the associations and they became non-significant.

Conclusions: Slightly elevated levels of hsTnT and hsTnI each add independent information if considered simultaneously to established risk factors and seem to have a similar long-term predictive value for subsequent CVD events in stable CHD patients.

P1320 | BEDSIDE
Troponin elevations following unselected invasive cardiac procedures: mortality in patients without myocardial infarction
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Purpose: A wide range of disease entities have been known to cause cardiac troponin elevations without myocardial infarction (MI). Yet no studies have investigated the prognostic implications of this condition in unselected pts undergoing invasive cardiac procedures. In this study we set out to assess the mortality risk in these pts.

Methods: We conducted a 1-year prospective study in unselected pts admitted to a university hospital. All pts who had cTnI measured because of a suspected MI were included. The decision limit for the diagnosis of MI was >0.03 ug/L. Pts with elevated cTnI, but who did not fulfill the criteria of the universal definition for MI, were categorized according to the underlying disease mechanisms.

Results: From January 2010 to January 2011 a total of 3762 pts qualified for inclusion. 1577 pts had cTnI elevations, of whom 488 had a MI. In 78 (7%) of the remaining 1089 pts, the elevations were caused by an invasive cardiac procedure (IP+). The 3 most common procedures were CABBG, aortic valve replacement and radiofrequency ablation (86/78). In 1101 non-MI pts, cTnI elevations were due to other conditions than invasive cardiac procedures (IP−). Median cTnI levels were 8.8 ug/L (IQR 3.8-16.1) for IP+ and 0.09 ug/L (IQR 0.05-0.20) for IP− pts (p<0.0001). During a median follow-up of 2.1 years, 550 pts died. Mortality differed between the groups: IP+ pts 10.3% and IP− pts 53.6% (p<0.001) (figure). In a multivariable Cox regression analysis the hazard ratio for IP− vs. IP+ pts was 2.0 (95% CI 1.5-2.6) compared with IP+ pts.

Conclusion: Pts with cTnI elevations caused by unselected invasive cardiac procedures, but without fulfilling the MI diagnosis, have a low long-term mortality, despite very high cTnI levels.

P1321 | BEDSIDE
The role of renal extraction in determining cardiac troponin T levels in chronic conditions and after acute myocardial injury
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Background: Cardiac troponin T (cTnT) in blood plays a pivotal role in the diagnosis of MI. Asymptomatic patients with a spectrum of renal function have been reported to have elevated levels of cTnT, when measured by a high sensitive (hs) assay, which has prognostic implications. Whether cTnT elevation is due to increased subclinical myocardial injury or decreased renal cTnT clearance is incompletely understood. Therefore, we sought to investigate the fractional renal extraction and cardiac production of cTnT at low baseline levels and after acute myocardial injury.

Methods: Ten men and 6 women undergoing electrophysiology ablation procedures were enrolled in this study. 15 patients had pulmonary vein ablation for atrial fibrillation and 1 patient had ablation for ventricular tachycardia. hs cTnT was measured at baseline, 30 days from the renal vein, radial artery and coronary sinus pre- and 43±34 minutes post last ablation.

Results: The mean creatinine and eGFR was 0.95±0.22 mg/dL and 84.7±25.3 ml/min/1.73m², respectively. Post-procedural values for cTnT were greater than <.
Cardiac output (r=0.154, p<0.001); figure). In multivariate Cox regression analysis the hazard ratio for pts with pneumonia was 2.1 (95% CI 1.2-3.5) compared with heart failure pts. Conclusion: Chronic kidney disease is the most prevalent condition causing cTnI elevations in unselected hospitalized pts without MI. Pneumonia comes second and is associated with a nearly 70% two-year mortality.

P1324 | BEDSIDE
Head-to-head comparison of MR-proANP and NT-proBNP in patients with stable coronary heart disease followed over 8 years
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Background: Pathophysiological studies suggest that A-type natriuretic peptides might provide valuable information beyond B-type natriuretic peptides about cardiac dysfunction in patients with CHD. The clinical performance of elevated circulating MR-proANP in a head-to-head comparison to NT-proBNP in unselected patients with stable CHD has not been evaluated.

Methods: Plasma concentrations of MR-proANP and NT-proBNP were measured at baseline in a cohort of 1,548 patients aged 30-70 years with CHD, and participating in an in-hospital rehabilitation program. Main outcome measures were cardiovascular mortality, non-fatal myocardial infarction, and non-fatal stroke.

Results: During a median follow-up of 8.1 years, 150 patients (incidence 21.1 pro 1,000 patient-years) experienced a secondary CVD event. MR-proANP was associated with a hazard ratio (HR) of 1.89 (95% CI 1.01-3.57) when the top quartile was compared to the bottom quartile in the fully adjusted model (p for trend 0.011). For NT-proBNP the respective HR was 2.22 (95% CI 1.91-4.14) with a p for trend of 0.0012. Finally, on top of a multivariate model including hs-troponin T, MR-proANP improved various model performance measures including c-statistics, and reclassification metrics, but without being superior to NT-proBNP.

Conclusions: MR-proANP and NT-proBNP show similar prognostic value in stable CHD.

P1325 | BEDSIDE
ProANP, changes in adiponectin during STEMI and prognosis
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Background: Natriuretic peptides (NP) have been suggested to regulate adipocyte metabolism including adiponectin. In patients with HF, intussusception of ANP increased plasma adiponectin. However, this has not been studied in a clinical setting or in myocardial infarction. Accordingly, we investigated the interplay between proANP and adiponectin and the prognostic implications in patients with STEMI.

Methods: We prospectively included 760 patients with STEMI treated with primary-PCI, from September 2006 to March 2011. Blood samples were drawn immediately before PCI, and in a subgroup (n=80) additionally three times. Plasma adiponectin and proANP were measured in all blood-samples. Endpoints were all-cause mortality (n=137) and the combined endpoint (n=188) of major adverse cardiovascular events (MACE).

Figure 1. Changes in adiponectin during STEMI.
P1329 | BESIDE

The impact of renal sympathetic denervation on office and ambulatory blood pressure levels in patients with true resistant hypertension and obstructive sleep apnea-the interim analysis

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Purpose: The aim of our ongoing study is to investigate the clinical utility of renal denervation (RDN) for the treatment of resistant hypertension (RHTN) coexisting with obstructive sleep apnea (OSA). Here we report an interim analysis of the primary end-point: blood pressure reduction at 3 months.

Methods: In 185 patients (73M, 112F, mean age 55.4±7.9, range 32-69yrs) with true RHTN (office systolic [SBP] 140-90 mmHg and daytime SBP average >135 mmHg on ≥3 antihypertensive drugs including a diuretic) coexisting with moderate-to-severe OSA (apnea/hypopnea index ≥15) were allocated to two groups: in 14 patients (7B, 7F, mean age 57.1±4.6, range 30-69yrs) RDN was performed and 16 patients (13M, 3F, mean age 57.1±4.6, range 50-65yrs) were assigned to control group. At baseline and at three months follow-up all patients underwent evaluation of office blood pressure (OBP) and an ambulatory blood pressure levels (ABP) by ABPM.

Results: The treatment and control groups were well matched in regard to baseline characteristics. At 3 months OBP levels in the RDN group reduced by 26/17 mm Hg (p<0.001/p<0.001), whereas they did not differ significantly from baseline in the control group (change of 2/3 mm Hg, p=0.369/p=0.132). Between-group differences in OBP change were significant at p<0.001 for both systolic and diastolic OBP respectively. At 3 months systolic OBP <140mmHg was noted in 14 patients in the RDN group and in 2 patients in the control group (73.7% vs. 12.5%, p<0.001). In ABPM 24h, daytime and nighttime ABP levels were reduced by -13/9 mmHg (p<0.001/p<0.01), -15/9 mmHg (p<0.001/p<0.01) and -11/8 mmHg (p<0.01/p<0.01) in RDN group. In the control group no significant changes in 24h, daytime and nighttime ABP levels were observed. Between-group differences in ABP were significant for daytime systolic and diastolic ABP levels (p<0.001/p<0.001) and for 24h systolic and diastolic ABP levels (p<0.001 and p=0.033, respectively) but not for nighttime ABP levels.

Conclusions: The interim analysis of the on-going study designed to evaluate the clinical utility of renal denervation in true resistant hypertension coexisting with moderate-to-severe OSA showed improvements in office and ambulatory blood pressure levels 3 months after the procedure.

P1330 | BESIDE

The risk to fail in RDN- the unfavourable role of accessory renal arteries

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Purpose: Among patients with drug resistant arterial hypertension (DRAH) renal artery variations are common in MRI prior to renal denervation (RDN). Further more bilateral denervation should be done to interrupt the spirally interfered renal cross talk in hypertension regulation. In contrast to concomitant main branches, performing RDN in pol artery is not recommended due to their small vessel dimensions. We thought the investigation of the occurrence of renal denervation (RF) in accessory arteries is a predictor for RDN success after 6 months.

Methods: We performed RDN (RF catheter system, Simplicity, Medtronic Co.) in 110 patients (58.1%, male, mean age 60.5±10.2yrs, BMI 32.1, 48.4% DM II, 6.0±1.2 hypertensive drugs). After 6 months 62 patients underwent a 24h ABPM to assess the RDN success related to their anatomically driven complete ness of RF ablation. Results: Prior RDN the entire study group possessed a mean office BP (OBP) 163±14/87±10 mmHg and a mean ABDM 154±10/85±9 mmHg. 12 of 62 patients (19.4%) offered accessory concomitant main or pol arteries which were not completely ablated. In comparison patients without anatomical anomalies showed a drop off in 24h OBP of -18±4/4.5±2mmHg, whereas those with aberrant arteries decreased by -12.8±3.4/mmHg in OBP (p=0.67). Thus, based on this results we stopped RDN for 42 of all patients (67.7%) responsible to the 62 RDN, 34 (54.8%) with anatomically normal renal artery constitution vs. 8 (12.9%) with double branches or pol arteries. The relative risk of patients with accessory vessels and incomplete ablation procedure to fail in RDN was 1.83 (p=0.19), Regarding

PHYSICAL ACTIVITY AND CAROTID ARTERIES

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Purpose: To investigate the effect of moderate to high intensity physical activity (PA) on morphology and function of carotid arteries and on carotid intima-media thickness (cIMT) by means of cross-sectional and longitudinal studies. Methods: We performed a systematic review of all publications and ongoing clinical trials and experimental studies available. Results: The effect of PA on the morphology and function of carotid arteries was studied in 23 studies and in 28 interventions. All intervention reports were of high quality and the majority of the studies could be considered as high quality. For the primary outcome variable (cIMT at the location of the common to external carotid artery bifurcation) the mean effect size was calculated at d = -0.08 (p < 0.001). In 15 studies the effect of PA on the intima-media thickness of the carotid arteries was investigated in healthy subjects, and in 7 studies the effect of PA on the intima-media thickness of the carotid arteries was investigated in patients with cardiovascular disease. The mean effect size was calculated at d = -0.09 (p < 0.001). In conclusion, moderate to high intensity PA is associated with beneficial effects on the morphology and function of carotid arteries and on carotid intima-media thickness. Nevertheless, further investigation is needed to elucidate the underlying mechanisms.
the RDN success no differences could be observed in capacity of applied power or number of ablation points between anatomic groups.

Conclusion: At RDN screening, accessory renal arteries are a common phe-
nomenon in patients presenting with DRAH. However, to fail to ablate these ves-
sels caused by small diameter or anatomical challenges is associated with an increased risk of an absent success of RDN after 6 months.

P1331 | BENCH
Evaluation of lesion and thermodynamic characteristics of Symplicity and EnligHTN renal denervation systems in a phantom renal artery model
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Purpose: Radiofrequency renal artery denervation has been used effectively to treat resistant hypertension. However, comparison of lesion and thermodynamic characteristics for different systems has not been previously described. We aimed to assess spatiotemporal lesion growth and ablation characteristics of Symplicity and EnligHTN systems.

Methods: A total of 39 ablations were performed in a phantom renal artery model using Symplicity (n=17) and EnligHTN (n=22). The phantom model consisted of a hollowed gel block surrounding a thermochromic liquid crystal (TLC) film, exhibit-
ing temperature sensitivity of 50-78°C. Flow was simulated using 37°C normal saline with impedance equal to blood. Radiofrequency ablations with each sys-
tem were delivered with direct electrode tip contact to the TLC.

Results: Lesion size was interpreted from the TLC as the maximum dimensions of the 51°C isotherm. Mean lesion depth was 3.82±mm ±0.04 versus 3.44mm ±0.03 (p<0.001) for Symplicity and EnligHTN respectively. Mean width was 7.17±mm ±0.08 versus 6.23mm ±0.07 (p<0.001), respectively. With EnligHTN, stability of lesion temperature was achieved 20 sec earlier, and was 15°C higher than Symplicity.

Conclusion: In this phantom model, Symplicity formed larger lesions compared to EnligHTN with lower catheter-tip temperature. The clinical significance of our findings needs to be further explored.

P1332 | BEDSIDE
Effects of renal sympathetic denervation on left ventricular structure and function: 1-year follow-up
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Background: Catheter-based sympathetic renal denervation (RDN) is an emer-
gent therapeutic option for patients with resistant hypertension. However, the impact of RDN in left ventricular (LV) structure is yet to be established. Our aim was evaluate the effects of RDN on LV structure and function (systolic and diastolic) in patients with resistant hypertension.

Methods and results: From a prospective registry of 49 consecutive patients with resistant hypertension submitted to RDN between July-2011 and February-
2014, all of them, by protocol, underwent an echocardiogram before and one year after RDN. The results are presented for patients with at least 1-year fup (n=24). Mean age was 63±7 years, 54% were men, the majority had hypertension lasting for more than 10 years (88%) and the median number of anti-hypertensive agents was 6. Left ventricular hypertrophy was present in all but 1 of these 24 pts. At 1-
year, there was a significant decrease on both systolic (181±5 to 152±12mmHg, p<0.001) and diastolic blood pressure (BP) (90±15 to 79±9mmHg, p=0.001). Regarding the 1-year echocardiogram, there was significant reduction in LV mass: 162±36 to 146±38g/m² (p=0.007) with no significant difference on the other evalu-
ated parameters (LV ejection fraction, E/e' ratio, E wave deceleration time and left atrial volume index). Reduction in LV mass achieved statistical significance only in BP responders (defined as a −10mmHg decrease in office systolic BP): n=19, 162±40 to 144±41g/m², p=0.003, vs 159±123 to 153±128 g/m², for non-responders; n=5, p=ns (figure).

Conclusions: In this population of patients with resistant hypertension submitted to RDN, blood pressure reduction was associated with a significant reduction in indexed left ventricular mass.

P1333 | BEDSIDE
Response or no response to renal sympathetic denervation - are there answers in exercise tolerance?
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Renal sympathetic denervation (RSD) in patients with drug resistant hypertension is a feasible procedure to strongly reduce office blood pressure as well as sinus rhythm heart rate at rest. Furthermore, studies have shown long term effects in exercise tolerance assessed in ergospirometry (CPET) in those patients who under-
RSD compared to non denervated hypertensive patients. However, it is still unknown whether differences exist between responders and none responding patients concerning their exercise tolerance.

Our study aim was to investigate whether exist differences in CPET parameters among RSD patients related to their RR response after 6 months.

Methods: Among a RSD cohort of 62 patients who underwent CPET at base-
line and after 6 months we selected 40 patients (60% male, 65±9 years of age, 5.8±1.5 antihypertensive drugs [AHDr]) divided in group 1 with 20 patients with the strongest response (in 24h ABDM) and in a group 2 with 20 patients without any response to RSD.

Results: Both groups presented comparable baseline parameters regarding medical history, number of AHDr (group 1: 5±1.0; group 2: 6±1.0; p=0.3) and base-
line office RR (OBP 161.5±88.3 vs. 170.7±78.4±). After 6 months, responders showed a decline in blood pressure at rest by -24±6/-4±3 mmHg, while OBP in none responders increased by 12±3/10±4 mmHg (p<0.001). Furthermore, responders tended to be more efficient (117±22 vs. 110±20 Watts), to have lower exercise RR (186±19±5 vs. 198±10/100±11±mmHg), a better peak oxy-
gen uptake (19.8±5.7 vs. 18.7±1.6 ml/kg/min) and a lower pulse pressure at rest and during exertion (p=0.6). At recovery after 1 minute, the systolic blood pres-
sure decline was more pronounced in group 1 vs. group 2 (25±8 vs. -19±9; p=0.13). Moreover, responders exhibited an improvement in heart rate recovery compared with patients who did not respond to RSD (p=0.06).

Conclusion: Patients successfully ablated by radiofrequency showed an im-
provement in their exercise capacity and exertional blood pressure rise accom-
panied by a favourable impact on prognostic parameters in drug resistant hyper-
tension like heart rate recovery and pulse pressure. Disappointing, the most of the CPET variables assessed showed still a tendency in favour of responders after RSD.

HUMORAL REGULATION OF BLOOD PRESSURE

P1334 | BENCH
Glucagon-like peptide-1 and blood pressure in young, healthy adults: a population-based study
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Purpose: Glucagon-like peptide-1 (GLP-1) not only plays an important role in the pathophysiology of impaired glucose tolerance, but is also correlated with blood pressure. The aim of this study was to assess the relationship of GLP-1 plasma levels and BP in young and healthy adults.

Methods: Healthy adults between 25 and 41 years of age without cardiovascular disease, diabetes or a body mass index >35 kg/m² were enrolled in a population-based study in the Principality of Liechtenstein. Total GLP-1, determined with research-use-only Single Molecule Counting technology assay, and ambulatory BP data were available in 1508 participants. Ambulatory BP monitoring was per-
formed over 24 hours using a validated device. Multivariable linear regression models were constructed to assess the relationship of GLP-1 with ambulatory BP.

Results: Median age of our population was 38 years. Median (interquartile range) GLP-1 levels across GLP-1 quartiles were 20.3 (16.6; 22.4), 27.6 (26.3; 29.8), 34.8 (34.8; 40.4) and 55.9 (50.0; 65.4) ng/L for men and 19.7 (16.2; 21.8; 28.2)

Abstract P1335 – Table 1. Systolic 24h BP, r (95% CI)

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<td>Fully adjusted</td>
<td>1.98 (0.98; 2.97)**</td>
<td>1.06 (-0.23; 2.36)</td>
<td>1.75 (0.45; 3.05)</td>
<td>2.82 (1.51; 4.13)</td>
<td>-0.0001</td>
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<tr>
<td>Fully adjusted with HOMA</td>
<td>1.70 (0.69; 2.55)</td>
<td>1.72 (0.45; 3.01)</td>
<td>1.54 (0.25; 2.83)</td>
<td>2.82 (1.51; 4.13)</td>
<td>-0.0001</td>
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<tr>
<td>Coefficients were adjusted for sex, age, body mass index, high-sensitivity C-reactive protein, physical activity, low density lipoprotein, high density lipoprotein, medication for hypertension, hemoglobin A1C, smoking, alcohol, body composition and education. Ref., Reference; HOMA, homeostatic model assessment insulin resistance. *p-value &lt; 0.01; **GLP-1 was log-transformed;</td>
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In hypertensive women, both the results of the screening for hyperaldosteronism and of the evaluation of insulin resistance depend on the timing of assessment in relation to the ovarian cycle

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We have reported that in low-renin hypertensive women the increment of plasma aldosterone that occurs in the luteal compared to the follicular phase of the ovarian cycle suggests the presence of an aldosterone-producing primary hyperaldosteronism (Yong J.Clin.Endocrinol.Metab, 2010). We here report the results of a study on 31 women in the fertile age evaluated because of arterial hypertension in whom both aldosterone and HOMA-IR index (glucose*insulin/405) levels were investigated during the ovarian cycle.

All measures (plasma aldosterone, PRA, insulin, glucose and progesterone levels) were done at the 5-7th (follicular phase) and 21-25th (luteal phase) day of the menstrual cycle, without hypotensive therapy or with doxazosin 4mg per day. All women reported a regular cycle, age 19-38 years (range:19-53 years), BMI 25.1±4.8 (19.3-35.8) kg/m².

Compared to the follicular phase, in the luteal phase plasma progesterone (P), aldosterone (ALDO), renin activity (PRA), insulin (I) and HOMA-IR all increased significantly: P from 0.61±0.3 to 8.7±4.1 ng/L (p<0.0001, t-paired); ALDO from 13.6±2 21.1±8 ng/dL (p<0.0001); PRA from 0.42±0.40 to 0.69±0.87 ng/mL/hr (p<0.02); I from 6.23±2.96 to 8.67±4.11 nM (p<0.0001); HOMA-IR from 1.39±0.8 to 2.01±1.21 (p<0.0001). For example, the proportion of ALDO: 15 ng/dL with ALDO/PRA<40 increased from 7.31 (23%) to 16.31 (52%); the proportion of HOMA-IR<2.5 increased from 3.22 (14%) to 6.22 (27%).

Multiple regression analysis demonstrated that P, but not ALDO and BMI were strong positive independent predictors of plasma insulin and HOMA-IR: univariate analysis 1) I vs P p=0.016; vs BMI p=0.0001; 2) HOMA-IR vs P p=0.065; vs BMI p=0.0001; multivariate analysis 1) I vs P (p<0.002) + BMI (p=0.0001); 2) HOMA-IR vs P (p=0.02) + BMI (p=0.0001).

These results in hypertensive women confirm that plasma aldosterone may greatly increase during the luteal phase of the ovarian cycle and suggest that also insulin resistance may increase to a greater extent than in normotensive women. This ovarian cycle is thus a source of variability of plasma aldosterone and of insulin resistance in hypertensive women in fertile age, with potential relevance in the diagnostic workup and pathophysiology of hypertension.
We aimed at investigating PBS pathophysiology at high-altitude, focusing on gender-related differences in chemosensitivity and by assessing the modifications of chemoreflex loop induced by acetazolamide.

**Methods:** 44 healthy lowlanders (21 females), randomized to acetazolamide/placebo, underwent polysomnography at sea-level and at 4559 m a.s.l. Hypoxic and hypercapnic chemoreflex sensitivities were assessed at sea-level.

**Results:** Males exhibited increased hypoxic chemosensitivity even after ventilation was normalized for body height (0.10±0.02 vs 0.08±0.02 L/min%/SpO2/m, p<0.001), and displayed PBS at altitude more frequently than females (40.9±27.8 vs 7.3±4.0 events/hour, p=0.008). Ventilation increased from sea-level to high-altitude (+4.6±2.1 L/min, p<0.001), irrespectively of gender and treatment. Acetazolamide leftward-shifted the CO2 set-point without gender-related differences and, at altitude, it improved oxygen saturation (p<0.001) during daytime (88.1±4.1% vs 77.2±4.6%) and nighttime (78.2±2.6 vs 71.4±4.3%) compared to placebo. The reduction (p<0.001) of end-tidal CO2 pressure from sea-level to high-altitude was more marked on acetazolamide than placebo (24.9±2.7 vs 29.9±3.0 mmHg, p=0.041). Acetazolamide at high-altitude resulted in less PBS in males (3.8±3.8 events/hour, p=0.002) and in females (2.9±3.5 events/hour, p=0.069), abolishing between-gender differences.

**Conclusions:** The greater severity of PBS displayed by males at high-altitude could be attributed to their higher chemosensitivity to hypoxia, promoter of ventilatory instability in context of hyperventilation-induced hypocapnia. Acetazolamide may attenuate BP-increase associated to altitude exposure by influencing the two sides of chemoreflex loop (modifying apneic threshold and improving oxygenation) and thus counteracting the occurrence of PBS in both genders.

**P1340 | BEDSIDE**

**Plasma reninase deficiency is associated with presence of arterial hypertension in patients after surgical repair of coarctation of aorta.**


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**Purpose:** The purpose of the study was to evaluate plasma reninase level (REN), a novel catecholamine-metabolising enzyme, in patients after surgical repair of coarctation of aorta (CoA) and among control volunteers in the context of underlying arterial hypertension (HA).

**Method:** The study comprised 50 consecutive patients after Dacron patch CoA repair (31 men (62%); aged 33 (26;40) years; HA in 29 (58%)). Both groups were stratified depending on the presence of HA. Plasma REN, C-reactive protein (CRP) and carotid intima-media thickness (IMT) were acquired in both groups.

**Results:** Plasma REN deficiency is associated with presence of arterial hypertension (HA) in both post-CoA patients and healthy controls.

**Conclusions:** Plasma reninase deficiency is associated with presence of arterial hypertension (HA).

**P1341 | BEDSIDE**

**Role of sympathetic overactivity and it’s relationship with diastolic parameters in resistant hypertensin.**


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**Purpose:** Sympathetic overactivity plays an important role in development of hypertension. In recent years, interventional therapies which targets the sympathetic system becomes popular for resistant hypertension. However, the effect of sympathetic predominance in resistant hypertensin is not very clear. In our study, we aim to evaluate the impact of sympathetic overactivity on resistant hypertension and its relationship with diastolic dysfunction.

**Method:** Among 218 patients enrolled; 57 were resistant hypertensivs, 83 were compared with hypertensive and 78 were normotensively. Mean heart rate and time domain heart rate variability (HRV) values (Standart deviation of NN intervals (SDNN), standard deviation of all 5 minute NN intervals (SDANN), root mean square of successive differences (RMSSD), Triangular index) which reflects sympathovagal overactivity were obtained from 24 hour ECG recordings. Transharcus echocardiography was performed and diastolic parameters (left ventricular (LV) mass, LV mass index, left atrial (LA) volume index) were assessed. HRV values were compared between groups. Association between HRV values and diastolic parameters was researched in resistant hypertensivs.

**Results:** In resistant hypertensiv group; mean heart rate (64.4±9 vs 71.9±9.1; p<0.001) was significantly higher; SDNN (114.4±10.3 vs 159.7±38.4; p<0.001), SDANN (107.4±5.07 vs 147.5±47.8; p<0.001) RMs (33.6±16.2 vs 47.8±21.7; p<0.001) and Triangular Index (29.7±10.2 vs 43.6±13.5; p<0.001) were significantly lower in resistant hypertensive group; mean heart rate (64.4±9 vs 74.1±10.6; p<0.001) was significantly higher, SDNN (114.4±10.3 vs 137.3±37.1; p<0.002) and Triangular Index (29.7±10.2 vs 36.10±9; p<0.006) were significantly lower than controlled hypertensive group. These results reflect chronic sympathetic predominance in resistant hypertension compared to both normotensive and controlled hypertensive state.

In controlled hypertensive group; SDNN (137.3±37.1 vs 159.7±38.4; p<0.001), SDANN (124.1±37.6 vs 147.5±47.8; p<0.004) and Triangular Index (36.10±9 vs 43.6±13.5; p<0.001) values were significantly lower than normotensive group. Among resistant hypertensivs; LV mass, LV mass index and LA volume index were significantly negatively correlated with SDNN and Triangular index.

**Conclusion:** Our study showed that sympathetic overactivity exists in hypertensive patients and this effect is more prominent in resistant hypertensivs. There is also a distinct correlation between sympathetic predominance and diastolic dysfunction in resistant hypertensive patients.

**P1342 | BEDSIDE**

**Impact of obstructive sleep apnea syndrome on plasma fibrin clot properties in patients with hypertension at high cardiovascular risk.**

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1Institute of Cardiology, Warsaw, Poland; 2Institute of Tuberculosis and Lung Diseases, Warsaw, Poland; 3 Jagiellonian University, Krakow, Poland.

**Purpose:** Formation of dense and poorly lysable plasma fibrin clots is observed clinical settings with high cardiovascular risk. Recently, it has been reported that in patients with obstructive sleep apnea (OSA), clot lysis time is prolonged. The aim of the present study was to investigate plasma fibrin clot properties in high cardiovascular risk patients with obstructive sleep apnea and without clinically overt cardiovascular disease.

**Methods:** We studied 87 hypertensive patients at high cardiovascular risk (according to the 2007 ESH/ESC criteria) suspected of OSA. Patients with previously diagnosed atherosclerotic cardiovascular disease were excluded. Fibrin clot properties including clot permeability (Ks), clot lysis time (CLT), and turbidimetric parameters of clot formation (the lag phase of fibrin formation and maximum absorbancy (Aabsmax) at 405 nm) were determined at the day of polysomnography.

**Results:** There were 49 patients (aged 49.9±18.8 years, 38M, 11F) with OSA (apnea/hypopnea index > 15 events/h) and 38 control patients (mean age 47.1±9.1 years, 22M, 16F) who did not differ with regard to age, sex, BMI and blood pressure. Patients with OSA had lower Ks (59.0±9 vs 75.7±1.2 10^{-9} cm²; p<0.001) and longer CLT (106.8±13.4 vs 90.5±15.1 min; p<0.001). In OSA patients clots tended to be formed faster (lag phase, 41.1±4.2 vs 43.2±5.6 s; p=0.061) and had higher Aabsmax (0.86±0.05 vs 0.84±0.08; p=0.11). KS and CLT correlated with AHI (r=0.56, p=0.001, and r=0.47, p=0.001; respectively) and mean sympathetic activity (r=0.30, p=0.005, respectively). In 14 patients with OSA fibrin clots properties that were evaluated before and after 3 months of CPAP treatment, an increase in Ks (6.1±1 vs 7.7±0.1 10^{-9} cm²; p<0.01), shorter CLT (106.1±10.8 vs 86.4±14.2; p=0.01), longer lag phase of fibrin formation (40.2±3.8 vs 44.7±4.0; p=0.009), and lower Aabsmax (0.86±0.05 vs 0.82±0.07; p=0.061) were observed.

**Conclusions:** In hypertensive patients with high cardiovascular risk, the presence of OSA was associated with unfavorable, prothrombotic changes in the structure and function of fibrin clots which significantly improve after CPAP treatment. The study suggests a novel prothrombotic mechanism in OSA which can be revers by CPAP treatment.
P1343 | SPOTLIGHT 
Relationship of vascular stiffness and sympathetic vascular tone with beat-to-beat systolic blood pressure variability in the elderly

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Purpose: To investigate the relationship of beat-to-beat Systolic Blood Pressure Variability (SBPV) with vascular stiffness, sympathetic vascular tone, and baroreflex sensitivity in elderly subjects aged 67-79 years old in orthostatic position.

Methods: Cross-sectional study, smoke- and diabetes-free elderly subjects (n=62) with and without hypertension (HTN), aged 67-79 years, female=34 (55%), HTN=26, in order to assess the association of use of chronic drugs. Blood pressure (BP) was measured in a sitting position (clinic SBP); then it was continuously monitored by photoplethysmography in supine position for 15 minutes at rest and during a 10-minute head-up tilt test. Supine and orthostatic autonomic modulation of systolic BP was assessed through spectral analysis of SBPV in the low (0.04-0.15 Hz) and high frequency (0.15-0.40 Hz) bands. SBPV was estimated by the standard deviation (SD) of beat-to-beat SBP values during 10 minute head-up tilt. Sympathetic vascular tone was estimated by LF-SBPV index. Vascular stiffness was assessed through planimetry on the radial artery. After computed generation of transfer function, augmentation index (Aix) was used to estimate vascular stiffness.

Results: Orthostatic SBPV was positively correlated with resting clinic SBP (r=0.22, p=0.042), AIX (r=0.308, p=0.007) and LF-SBPV (r=0.325, p=0.005), whereas there was a negative correlation with BRS LF (r=−0.290, p=0.01). Additionally, clinic SBP Aix, LF-SBPV were positive independent predictors of orthostatic SBPV (B=0.04±0.02, p=0.03, R2=0.08; B=0.08±0.03, p=0.02, R2=0.18; B=0.06±0.02, p=0.04, R2=0.28, respectively) after adjusting for age (table 1).

Conclusion: Clinic SBP, vascular stiffness, and sympathetic vascular tone are associated with increased beat-to-beat SBP in normotensive and hypertensive subjects aged 67-79 years old. These factors can be used to identify elderly patients with increased orthostatic SBPV.

P1344 | BEDSIDE
Rapid blood pressure increase in young middle age predicts decreased autonomic function at 60-64 years in the British 1946 birth cohort

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Purpose: Decreased vagal function and increased sympathetic function, reflecting a disturbance in the autonomic nervous system, have been associated with increased mortality in both healthy adults and in those with prevailing cardiovascular diseases. The mechanisms for these autonomic disturbances are less known, but humoral, central nervous factors, as well as afferent effects via baroreceptors which can influence blood pressure regulation might be implicated. In this study we set out to assess whether blood pressure change at a particular period during adulthood can influence blood pressure regulation might be implicated. In this study we set out to assess whether blood pressure change later in life, or even with current blood pressure. This stresses the importance of early prevention of blood pressure increase, and indicates that early middle-age SBP screening might be important for assessment of future CV risk.

ADVANCES IN CONGENITAL HEART DISEASE

P1346 | BENCH
3’UTR SNPs and haplotypes in GATA4 gene contribute to the genetic risk for congenital heart disease

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Background: Single nucleotide polymorphisms (SNPs) in 3’ untranslated region (3’UTR) of GATA4 gene may contribute to the pathogenesis of congenital heart disease (CHD) by altering miRNA gene regulation. We analyzed the association between SNPs and haplotypes in the 3’UTR region of the GATA4 gene and CHD risk.

Methods: SNPs located within the 3’UTR of GATA4 gene were analyzed for putative miRNA-binding sites, using bioinformatics algorithms, calculating the difference in Free Energy of hybridization (ΔFE, kcal/mol) for each wild-type versus variant allele. The sum of all ΔFE (ΣΔFEtot) was calculated in order to predict the biological importance of SNPs binding more miRNAs. The selected SNPs were genotyped in a case-control association study of 150 CHD patients and 250 healthy subjects. The haplotypes were evaluated using SNPAnalyzer (http://snp.istech21.com/snpanalyzer/2.0) and SNPStats (http://bioinfo.iconcology.net/SNPstats).

Results: Bioinformatics analysis indicated 4 SNPs (+1158 C>T, +1256 A>T, +1355 G>A, +1521 C>G) with ΔFEtot = 9.91, 14.85, 11.03, 21.66 respectively. Two SNPs (+1158 C>T and 1521 C>G) were found to be significantly associated with CHD risk (p=0.011 and 0.009 respectively). Haplotype analysis showed that the more common haplotype CAGC (Figure) increased the risk of CHD (p=0.014). Conversely, the TTCC haplotype (more uncommon in CHDs) was associated with a significantly decreased risk of developing CHD (p=0.035, see Table). Computational analysis showed that the presence of +1158 T can potentially create a binding site for putative miR-3162-3p, while the presence of +1256 T can destroy the binding site for putative miR-365-5p.

Conclusion: 3’UTR SNPs and haplotypes in GATA4 gene are new genetic factors for CHD, likely by altering miRNA gene regulation.

P1347 | BENCH
Persistent vascular remodeling related to development of arteriosclerosis or atherosclerosis in Kawasaki disease - Immunohistochemical study using an animal model


Background: Atherosclerotic coronary heart disease has recently emerged as a clinical issue among young individuals with a history of Kawasaki disease (KD), which is a systemic vasculitis unique to children. However, whether or not and how KD promotes arteriosclerosis remains unclear. We hypothesized that, analogous to the pathogenesis of arteriosclerosis or atherosclerosis, endothelial injury and the resultant intimal thickening are induced in coronary arteries after attenuation of vasculitis.

Methods: We used a rabbit model of KD developed by Onouchi and performed histopathological analysis of arteries at acute (1, 3, 5, and 7 days) and chronic (3 months) phases of the disease.

Results: In these rabbit models, a pan-arteritis with significant intimal cellular hypertrophy was histologically detected in the acute phase, and arterial intimal thickening was observed during the early chronic phase. Immunohistochemical analysis of the coronary arteries revealed that the thickened intimal lesions observed during the chronic phase comprised abundant α-smooth muscle actin (α-SMA)-positive cells, most of which concomitantly expressed vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1) in an endothelial cell-like manner. Although macrophages positive for RAM1 were barely detected, macrophage colony stimulating factor was strongly expressed in migrating smooth muscle cells in the intimal layer. In addition, the accumulation of proteoglycan as extracellular matrix was distinctly visible in the thickened intima,

function at 60-64 years, and is more closely associated with autonomic dysfunction than blood pressure change later in life, or even with current blood pressure. This stresses the importance of early prevention of blood pressure increase, and indicates that early middle-age SBP screening might be important for assessment of future CV risk.
Methods: This prospective study on QoL was conducted since 2005 in a cohort of life (QoL). Most studies on QoL lack longitudinal follow-up. This study aimed to

Patients with pulmonary arterial hypertension due to congenital heart

Background: Haemodynamics after the Fontan procedure is very different compared with that in healthy individuals, but in many cases, the procedure poses no hindrance to daily lifestyle. Exercise tolerance after the Fontan procedure differs according to the type of the operative procedure, with total cavopulmonary connection (TCP) resulting in a better exercise tolerance than atrio pulmonary connection (APC). However, few detailed studies have examined how biological reactions change over the course of exercise.

Methods: The subject comprised 4 patients who had undergone the Fontan procedure (2 patients each for APC and TCP) and 2 healthy volunteers. Subjects performed a 15-minute exercise test on an ergometer and were assessed at rest. Assessment items included heart rate (HR), blood pressure (BP), Spo2, cardiac function (cardiac index (CI) and cardiac contractile force coefficient (ICON)) using a non-invasive cardiac output monitor and biomarkers (NT-proBNP, ANP and aldosterone).

Results: HR, BP, CI and ICON increased in all subjects during exercise, but the rate of increase was lowest in case of APC patients. ANP was increased through exercise in all subjects, and peak values were highest in APC patients. In addition, values returned to those at rest after 1 hour in all subjects except for APC patients, who showed no recovery (Fig. 1A). Aldosterone was increased after exercise in healthy controls and APC patients, but no change in TCP patients (Fig. 1B).

Conclusion: When changes in biological reaction and biomarkers were compared during exercise, patients who had undergone TCP had better Fontan haemodynamics than APC patients and TCP in particular showed temporal changes comparable with those of healthy individuals.

Longitudinal changes in quality of life predict mortality in adult patients with pulmonary arterial hypertension due to congenital heart disease

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Purpose: Patients with pulmonary arterial hypertension due to congenital heart defects (PAH-CHD) have high morbidity and mortality rates, affecting their quality of life (QoL). Most studies on QoL lack longitudinal follow-up. This study aimed to assess quality of life over time and to determine its predictive value for mortality.

Methods: This prospective study on QoL was conducted since 2005 in a cohort of adult PAH-CHD patients, starting advanced therapy treatment. Short-form QoL health surveys (SF36) were recorded at baseline and at follow-up visits (median 4 years). We investigated the association between QoL, divided in a physical and mental score, and mortality using logistic regression. Change in QoL was calculated as the difference between first and last available SF36 score.

Results: In total 196 questionnaires were analyzed from 61 patients with PAH-CHD (mean age 43±13 years, 43% male, 34% Down syndrome). Fourteen patients died (23%). The mean standardized SF36 physical score was decreased (35 vs 50 in a standardized healthy US population), in contrast to the mean mental score (51 vs 50). Patients who died showed declining physical (-4.3) as well as mental scores (-5.8). In univariate regression decline in SF36 physical score was a determinant for mortality (OR 7.3; 95%CI 1.3-40.4; p=0.02).

Conclusion: Decline in longitudinal course of SF36 physical scores are predictive for mortality.

Emergencies due to unrecongnised aortic coarctation in adults

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Objective: Data on the extremely rare cohort (survivors in whom adulthood was emergently complicated due to unreco gnised aorta (CoA)) are missing.

Methods: The study—retrospective, cross-sectional, descriptive. The cohort = all adults with the CoA who were (2000-2012) under the care in the university cardiovascular centre with the special view on emergencies in adults due to unrecon gised (EAU) CoA. Data collection (database + interview) = 1. emergencies-type, age, resolution, repetition; 2. potential risks—residues, foreign metallic cardiovascular material; 3. others.

Results: The whole group (Fig. 1): 54 adults (35±18 (83 years, 60% men). In 26% (14/54 pts) the diagnosis of CoA was made in adulthood—importantly in 64% (9/14 pts) importantly (34±19 years). Description of this EAU CoA subgroup (9 pts): emergencies occurred once per 6.1 years sooner in men (25±8 years) when comparing women (46±23 years). Emergencies were: acute heart failure (33%; both genders), spinal complications (33%; men), aortic complications (11%; man), hypertensive crisis (22%; women). Except one woman refusing any interventions, other emergencies (8/9 pts) were resolved surgically. In this EAU CoA subgroup the second emergencies were in 44% (4/9 pts; follow-up 20±8.9 y (years); cardiac arrest, aortic dissection, acute heart failure). In the EAU CoA subgroup there were also in 33% (3/9 pts) non-surgically treated complications (endocarditis, systolic dysfunction) and 75% (3/4) of EAU CoA women became a mother—prior the diagnosis of CoA.

Prevalence of coronary artery anomalies in patients undergoing coronary artery angioigraphy: a review of 16768 patients

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Objective: In our study, prevalence of CAAs in coronary artery angiography (CAG) performed patient group is aimed to be detected by investigating images in a tertiary healthcare provider.

Background: Coronary artery anomalies (CAAs) existing as of birth and they are coincidently detected most of the time.

Methods: Images of 16.768 CAG performed patients in our hospital were evaluated regarding CAA.

Result: CAAs were detected in 120 cases (0.7%). Anomalies of originat and course was observed in 86 cases (70.1%). Absence of LMCA was spotted in 59 cases (49.9%) as the most frequent anomaly in subgroup analysis of these cases. Anomalous location of coronary ostium outside normal coronary sinuses was determined in 20 cases (16.6%). In analysis of these 20 cases; arising Cx from right sinus of valsalva was observed in 8 cases (6.6%) as the most frequent abnormal exit anomaly. Arising Cx from RCA was seen in 6 events (5%), arising RCA from left sinus of valsalva was seen in 4 events (3.3%) and arising LMCA from right sinus of valsalva was seen in 2 events (1.6%) constituted other exit anomalies.

Conclusions: In our study, absence of LMCA was the most frequently encoun-
tered anomaly. Although CAAs are rare cases, they can cause difficulties in CAG interventions and surgical operations. In our study, frequencies of CAAs are presented in CAG performed patients.

P1352 | BEDSIDE
Adults with congenital heart disease have lower habitual physical activity level compared to healthy age and gender matched controls

Material and methods: Eighty-three adults (34 women, mean age 37.0±15.0) with CHD, classified as either “complicated” (n=25) or “uncomplicated” (n=58), and 41 age and gender matched healthy controls (16 women, mean age 37.0±15.1) were studied with a combined uniaxial accelerometer and heart rate monitor that was applied on the chest and worn during 5 consecutive days. They were encouraged to proceed with their usual activities. A validated algorithm based on individual age, gender, height and weight converted data into time spent in different metabolic equivalent (MET) levels during an average monitored day. Based on the national recommendations on physical activity of at least 150 min/week (0.57 equivalent (MET) levels during an average monitored day. Based on the national recommendations on physical activity of at least 150 min/week (0.57 MET) vs. 68 MET) and EQ-5D index=1 (95% CI 1.02-1.06) and EQ-5D index=1 (p=0.024) in patients with simple lesions and 14.6% (n=6, p=0.003) in healthy controls.

Background: Most adult patients with congenital heart disease have reduced aerobic exercise capacity. Their habitual physical activity level is however less studied. The aim of this study was to investigate the habitual physical activity level in a cohort of adults with congenital heart disease (CHD) compared to healthy controls.

Results: Adults with complex CHD were less physically active at moderate intensity (3-6 MET) compared to healthy controls (0.57±0.59 vs. 0.99±0.68 MET hours, p=0.015). Fifty percent (n=21) of the patients with a complex lesion did not reach the national recommendations of physical activity, compared to 22% (n=9, p=0.024) in patients with simple lesions and 14.6% (n=6, p=0.003) in healthy controls. In a multivariable logistic regression model higher MMR (p=0.001; OR 1.94; 95% CI 1.02-3.68), and EQ-5D index=1 (95% CI 1.02-1.06) and EQ-5D index=1 (p=0.024) were independently associated with physical activity above the recommended level.

Conclusion: Many adults with complex CHD have lower habitual physical activity level compared to healthy age and gender matched controls. Their habitual physical activity level is however less studied. A validated algorithm based on individual age, gender, height and weight converted data into time spent in different metabolic equivalent (MET) levels during an average monitored day. Based on the national recommendations on physical activity of at least 150 min/week (0.57 MET) vs. 68 MET), which included 31 atrial septal defect, 21 patent ductus arteriosus, 8 ventricular septal defect and so on (Table). A serious case of Bland-White-Garland syndrome was detected and immediately sent to hospital.

P1353 | BEDSIDE
Multicenter registration for fetal echocardiography in Japan
K. Takigiku1, H. Kamino2, M. Karnei3, S. Yasukochi1.

Table 1. Prevalence data according to the basic classification in angiography and anomaly population

<table>
<thead>
<tr>
<th>Anomalies of orgination and course</th>
<th>Prevalence of angiography population (n=16,768)</th>
<th>Prevalence of anomaly population (n=1,120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anomalies of intrinsic coronary artery anatomy</td>
<td>86</td>
<td>0.006%</td>
</tr>
<tr>
<td>Anomalies of origin termina</td>
<td>18</td>
<td>0.001%</td>
</tr>
<tr>
<td>Anomalies of coronary artery</td>
<td>16</td>
<td>0.090%</td>
</tr>
<tr>
<td>Anomalies of anomalous vessels</td>
<td>0</td>
<td>0.00%</td>
</tr>
</tbody>
</table>

Background: Nationwide multicenter registration for fetal echocardiography leading definitive diagnosis, not screening, was started in September 2004 in Japan. Japanese Society of Fetal Cardiology endorsed the registration and performs a key role for understanding and investigation of the current situation.

Subsequent 15-years on-line registration for the definitive diagnosis using fetal echocardiography enrolled from 1 October 2004 to 25 December 2013. We investigated the ratio of the registrations in accordance with the annual changes of registrations, the number of registrations in each prefecture and classification of diseases.

Result: The number of registrations increased year by year. There were only 1,400 registrations until 2009, which increased to more than 2,000 registrations after the year. As for the classification of diseases, 7,233 cases were reported as a left ventricular outflow tract defect, which accounted for 46%. For the rest, 37% showed normal conditions, and 7% caused an arrhythmia and some extracardiac abnormalities. The percentages remained almost unchanged throughout the years. By prefecture, there were 2,677, 2,384, 2001 and 1,561 registrations in Osaka, Tokyo, Kyoto and Nagano, respectively. Less than 50 registrations, however, had been made for the 9 years in 18 prefectures. The congenital heart defect reports consisted of 1,271 cases of VSD (8%), 329 cases of SRV, 94 cases of SLV, 678 cases of DORV, 618 cases of HLHS, 618 cases of AVSD and 563 cases of TOF; thus, many of the abnormalities tended to be found on the four-chamber view. A minority of cases included 352 cases of dTGA (2.2%), 447 cases of COA, 104 cases of IAA. In particular, only 33 cases of TA PVC were reported and those were 1% of all. Regarding the arrhythmia, there were 408 cases of PAC (2.6%), 130 cases of complete atrioventricular block, 102 cases of PVC, 88 cases of PSVT, 53 cases of AFAV and 40 cases of VT.

Conclusion: Nowadays, the number of registrations tended to increase, and finally 15,000 registrations were achieved. Many of the diseases, which could be detected on the four-chamber view easily by screening, were diagnosed definitively. It is obvious that most of Japanese Society of Fetal Cardiology, as a key player, demonstrates the significance in the screening results.

P1354 | BEDSIDE
Echocardiographic screening for congenital heart disease in infants and preschool children: 12 years experience in a civic event for children care
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Background: Fetal echocardiography has been performed for the early prenatal diagnosis of major congenital heart disease (CHD) and cardiac screening for neonates and infants is usually performed by auscultation. However, CHD can be diagnosed in school age or adulthood sometimes in advanced stage. We had chance to perform echocardiographic screening for infants and preschool children on behalf of the prefecture of our area for children care which our prefecture held once a year for their healthy life.

Methods: Subjects consisted of 8819 infants and preschool children (1 month to 6 year-old) underwent echocardiographic in the public event from 2001 to 2013. Children with known CHD were excluded. The event opens 2 days in every year except 2010 for an epidemic of a severe acute respiratory syndrome.

Results: We performed echocardiographic screening on 735144 children in each event. In totally 12 events, subjects consisted of 3175 0-year-old (36%), 2292 1-year-old (26), 1058 2-year-old (12%), 794 3-year-old (9%), and others. In all subjects for 12 events, we could identify echocardiographic abnormality in 137 children (1.6%), which included 31 atrial septal defect, 21 patent ductus arteriosus, 8 ventricular septal defect and so on (Table). A serious case of Bland-White-Garland syndrome was detected and immediately sent to hospital.

Conclusion: Cardiac abnormality, which could not be pointed out by prenatal echocardiography and neonatal auscultation, could be identified in substantial number of neonates and infants by echocardiographic screening. Echocardiographic screening in infants may be useful for early diagnosis of CHD in the country where its birthrate is declining.

P1355 | BEDSIDE
Impact of early initiation of intravenous prostanooid therapy in patients with congenital heart disease-related pulmonary arterial hypertension

Purpose: Pulmonary vascular disease can complicate large intracardiac shunt lesions, precluding the possibility for surgical repair. Advanced oral therapy (AOT) is safe and effective in these patients. Intravenous therapy is less utilized due to fears of infection and paradoxical embolism; the impact of this choice is uncertain.

Methods: We compared outcomes of patients with congenital heart disease-related pulmonary arterial hypertension (CHD-PAH) initially treated with AOT (endothelin receptor antagonists and phosphodiesterase-5-inhibitors) to those initiated on intravenous prostanoids (IP). We identified 51 patients with CHD-PAH from a prospectively collected database of over 800 patients with PAH presenting between 1998-2010 to a tertiary center (10) and who function class were also similar (II or IV in 53% vs 52%), though mean pulmonary artery pressure (50±23 vs. 68±19 mmHg, p=0.006) and pulmonary vascular resistance (8.4±8.2 vs. 15.6±10.6, p=0.009) were higher in the IP patients. Use of additional therapies

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P1356 | BEDSIDE

Mortality is predicted by small area of common chamber at birth in asplenia patients with total anomalous pulmonary venous connection

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Introduction: We know asplenia patients with total anomalous pulmonary venous connection (TAPVC) have worse prognosis if they have small common chamber. This study assessed whether mortality was estimated by preoperative area of common chamber (Pre-CC) for asplenia with TAPVC before 1st palliation.

Methods: The medical records of 14 asplenia with TAPVC were reviewed. They underwent high-resolution computed tomography (HRCT) before 1st palliation between 2004 and 2011. Pre-CC was calculated as ellipsoid between upper and lower pulmonary veins. The area under a receiving operating characteristics (ROC) curve was calculated to determine the best discriminating Pre-CC for predicting mortality. Each index was calculated for predicting mortality. Next, we examined whether 2nd PreCC before 1st palliation was associated with mortality.

Results: HRCT were performed at median 0 day. Pre-CC was between 3.6mm² and 23.6mm². Eight died eventually. Descriptive features at birth which were turned up by means of daily clinical practice, such as level of oxygen saturation, cardiovascular ratio, and degree of pulmonary congestion, were not different between mortality group and non-mortality group. In addition, the ratio of mortality was not related to morphological and functional differences: TAPVC type; pulmonary artery morphology; degree of atrio-ventricular valve regurgitation; existence of ventricular dysfunction. Only small Pre-CC was associated with mortality (10.6mm² vs. 21.6mm², p=0.014). The area under ROC curves of Pre-CC for predicting mortality was 0.85 (p<0.028). ROC curve analysis confirmed 16.3mm² as the best diagnostic cut-off value. Sensitivity of small Pre-CC (≦16.3mm²) for predicting mortality was 88%; specificity 83%; negative predictive value 83%; positive predictive value (PPV) 88%. Seven patients had 2nd HRCT before 1st operation. Three patients had Pre-CC under 16.3mm² at 1st time. Although two of them had Pre-CC over 16.3mm² at 2nd time, they all died. Four patients had PreCC over 16.3mm² at 1st time. Although two of them had Pre-CC under 16.3mm² at 2nd time (47%), they all survived. Conclusion: Our study showed there were no significant factors other than Pre-CC which predict mortality in asplenia patients with TAPVC before 1st palliation. Small Pre-CC must be firmly attributed to obstructive lesions of pulmonary vascular bed in fatal life. Modification of obstructive lesion would be only temporal after birth. We might estimate 2nd time, they all survived.

P1357 | BEDSIDE

Grown-up congenital heart disease intensive care admissions: an 8-year experience

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In response to reduced health funding due to the current economic crisis, in 2013 NHS England began to reorganise cardiac services in the London region to control clinical expertise and reduce costs. This approach is likely to be rolled out throughout the remainder of the UK and abroad. As increasing numbers of congenital heart disease patients survive until adulthood, there will be an increase in hospital admissions with pressure on general intensive care units (ICU) to care for these patients with no onsite grown-up congenital heart disease (GUCH) team. To assess the ICU need of GUCH patients, we reviewed admissions to the ICU at our tertiary centre.

Coded data was used to identify patients with congenital heart disease who had been admitted to intensive care from 2005 to 2013 who were under the care of the grown-up congenital heart disease team. The electronic database was then reviewed to identify age, sex, admission duration, reason for admission and complications.

513 ICU admissions were identified from 501 patients. 434 (85%) were following elective or emergency cardiac surgery and as such were not looked at further; these patients would continue to be operated on at a specialist centre. Of the remaining 79 (15%) admissions, 37 (7%) were admitted to the general ICU, 22 as an emergency, 11 following elective non-cardiac surgery and 4 were transferred from the cardiac ICU for prolonged respiratory weaning. 42 (8%) patients were admitted to the cardiac ICU, 26 as an emergency, and 16 following elective non-cardiac surgery. Mean age of the admissions was 37 years, (standard deviation (SD) 14), 49% were female. Mean ICU stay was 7.9days (SD 13.7), mean hospital stay 25.8days (SD 30.5). The most common diagnoses were tetralogy of Fallot (13, 16%) and transposition of the great arteries (12, 15%), aortic stenosis, atrial septal defects, coarctation and pulmonary atresia accounted for 4 (5%) patients each. 14 (22%) patients died during their admission, 4 (8%) were transferred to the wards, 17 (28%) were transferred to the cardiac ICU. The outcomes of grown-up congenital heart disease patients treated for these conditions were comparable to other specialties. The most common cardiac arrest (15, 19%), acute kidney injury (12, 15%) and pneumonia (8, 10%). Despite the majority of GUCH patients being admitted to a cardiac ICU following elective cardiac surgery, a considerable portion of our GUCH patients would have required admission to a general ICU. These patients are intensive users of health facilities. Clinical leads will have to plan for this change in service provision as general ICUs may see a larger number of GUCH patients unless a dedicated referrals system exists for these patients.

ACUTE PULMONARY EMBOLISM AND BASIC SCIENCE IN PULMONARY ARTERIAL HYPERTENSION

P1359 | BEDSIDE

TIMI Risk Index calculated at hospital admission predicts both in-hospital mortality and all cause mortality at follow-up in acute pulmonary embolism

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Introduction: TIMI Risk Index (TRI) is a friendly user prognostic assessment tool that is used to predict 30 day mortality in patients with STEMI and NSTEMI. It is based on simple clinical and demographic data: age, heart rate and systolic blood pressure. In this study, we know that TRI is also a strong predictor of other variables that are independent prognostic factors in other cardiovascular acute diseases like acute pulmonary embolism (APE). TRI has not yet been tested to assess prognosis in APE.

Objective: This study aims to assess the prognostic impact of TRI calculated at hospital admission on both in-hospital and after discharge prognosis in patients with APE.

Methods: Retrospective, observational study that included all patients with APE diagnosed during emergency room stay by MDCT between January 2010 and December 2011. The primary endpoint was all cause in-hospital mortality and the secondary endpoint was all cause death after discharge. A receiver operating characteristics (ROC) curve was used to test TRI as a predictor of the primary endpoint and to obtain the best cut-off value. Regression analysis were done to assess strength of prediction.

Results: Between January 2010 and December 2011, 436 patients (205 males, mean age 72 years) were diagnosed with APE. 46 (10.6%) patients died during hospital stay. Means of TRI were significantly different between patients that died during hospital stay (TRI mean 51.46, sd 23.00) and patients that survived (TRI mean 37.78, sd 17.49, p=0.012). A value of TRI higher than 34 was found to be strongly associated with a worse in-hospital prognosis (unadjusted OR 6.64, 95% CI 2.30-19.18, p<0.01). Only TRI greater than 34 significantly contributed to the prediction model (TRI greater than 34 adjusted OR 18.572 (95% CI 2.457-140.400), p=0.005, troponin level adjusted OR 1.723 (95% CI 0.899-3.001), p=0.055). During follow-up, of 280 patients 50 died (11.5%). Means of TRI were also statistically different between patients that died during follow-up after- discharge (TRI mean 43.58, sd 15.84) and patients that were still alive (TRI mean 36.24, sd 17.78), p=0.012. A value of TRI higher than 34 was found to be associated with a lower event free survival (hazard ratio 2.257 (95% CI 1.195-4.261), p=0.012).

Conclusion: TRI is a predictor of both in hospital mortality and all cause mortality at follow-up after APE.
for the period December 2012 - August 2013, 14 patients with acute pulmonary embolism and hemodynamic instability were treated with local fibrinolysis, rotational thrombus fragmentation and thrombus aspiration.

Methods: All 14 patients were with PE and hemodynamic instability and echocardiographic evidence for RV dysfunction. The mean time from the beginning of symptoms was 3.2 days. One patient died before the procedure and was excluded from analysis. The procedure in all patients was performed in the first 12 hours from hospitalization. We used right or left femoral vein for access site with insertion of 8 Fr sheath. After insertion of 5 Fr Pigtail catheter a selective pulmonary arterial injection was made. Then consecutively in the right and left main branch a local administration of alteplase 25 mg was performed through the Pigtail catheter. With 0.035 inch guidewire through the pigtail a rotational thrombus fragmentation was performed. Then a precise selective angiography was made with 8 Fr catheter in all segments of the pulmonary arterial tree with diameter above 6 mm. A meticulous thrombus aspiration was then performed in all segmental branches that were involved through the same catheter.

Results: From the analyzed 13 patients 66.7% were male with a mean age of 57 years. The in-hospital survival was 92.3% as only one patient died due to lung infection. We also evaluated the 24 hours effect from the procedure. There was an increase in both O2 saturation (92.1% vs 97.6%, p=0.008) and PO2 (67.8 vs. 114.5 mm Hg, p=0.002). The right ventricular basal diameter decreased (49 mm vs. 38 mm, p=0.009) and the systolic function (tricuspid annular plane systolic excursion decreased from 13 mm vs. 19 mm p=0.011). The systolic (62 mmHg vs. 62 mmHg p=0.03) and mean (51 mmHg vs. 41 mmHg, p=0.034) PA pressure also decreased. At 8-12 months follow-up all patients were alive with sustained clinical and echocardiographic result with no residual pulmonary hypertension.

Conclusion: Our experience showed that the described manual technique is a feasible, effective and save method for treatment of high risk patients with pulmonary embolism. Our method permits decrease of overall used dose of lytic agent combined with effective mechanical removal of thrombus material.

P1361 | BEDSIDE
Atrial fibrillation prognostic score CHA2DS2-VASC may be used to assess prognosis after discharge in acute pulmonary embolism

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Introduction: A recent retrospective cohort study of patients with acute pulmonary embolism (APE) has showed that the atrial fibrillation score CHA2DS2-VASC was also a valid tool to assess long term prognosis in APE patients.

Objective: This study aims to assess the prognostic impact of CHA2DS2-VASC calculated at hospital admission on after discharge prognosis in patients with APE diagnosed by MDCT during emergency room stay.

Methods: Retrospective, observational study that included all patients with APE diagnosed during emergency room stay by MDCT between January 2010 and December 2011. The primary endpoint was all cause death after discharge. We used the CHA2DS2-VASC score to calculate the 30-day mortality. Both variables significantly contributed to the prediction model (belonging to group 1 adjusted OR=8,57 (95% CI: 2,65–27,72), p<0.001, troponin level adjusted OR 1,60 (95% CI: 1,06–2,42), p=0,026). During follow-up, all cause mortality was significantly higher for group 1 patients (hazard rate 4,02 (95% CI: 1,89–8,55, p<0.001).

Conclusion: Atrial fibrillation prognostic score CHA2DS2-VASC was statistically higher in group 1 (13,02 vs. 24,47, p=0,002), higher PCR (9,94 vs 8,79, p=0,023, higher D-dimer (24,47 vs.54,38 vs. 8,79, p<11,82, p<0,001), lower troponin (11,67 vs 2,19 vs 13,02±1,19, p<0,001) and lower hemoglobin (9,19 vs. 6,47, p=0,023). The right ventricular basal diameter decreased (49 mm vs. 38 mm, p=0.009) and the systolic function (tricuspid annular plane systolic excursion decreased from 13 mm vs. 19 mm p=0.011). The systolic (62 mmHg vs. 62 mmHg p=0.03) and mean (51 mmHg vs. 41 mmHg, p=0.034) PA pressure also decreased. At 8-12 months follow-up all patients were alive with sustained clinical and echocardiographic result with no residual pulmonary hypertension.

Conclusion: Our experience showed that the described manual technique is a feasible, effective and save method for treatment of high risk patients with pulmonary embolism. Our method permits decrease of overall used dose of lytic agent combined with effective mechanical removal of thrombus material.
were randomised to control (CON), ischemic preconditioning (IPC, 2 x 5 min of global ischemia), or addition of the PDE5 inhibitor vardenafil (VARD, 60μM), the cGMP-dependent protein kinase (PKG) blocker KT 5823 (1μM) or vardenafil plus KT 5823. Drugs were added to the perfusion buffer five minutes prior to global ischemia. The interventions were followed by 40 min of global ischemia and 120 min of reperfusion in all groups. The effects of IPC on the right ventricle were evaluated by measurement of the infarct size/area-risk ratio (IS/AAAR).

Results: Ischemic preconditioning reduced infarct size in the RV. A cardioprotective effect similar to ischemic preconditioning was seen for the PDE5 inhibitor vardenafil. The PKG blocker KT 5823 abolished the cardioprotective effect of vardenafil. KT 5823 alone did not have any effect on infarct size. (Fig.1).

Conclusion: PDE5 inhibition by vardenafil protects the right ventricle against ischemia. This effect is abolished by blockade of PKG suggesting that PKG is a key mediator of the cardioprotective effects of vardenafil in the right ventricle.

P1365 | BENCH
Echocardiographic prediction of pre- versus post-capillary pulmonary hypertension

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Background: The differential diagnosis between pre- and post-capillary pulmonary hypertension (PH) is of major therapeutic relevance, and thus requires an optimal clinical probability assessment with use of echocardiography.

Methods: We reviewed the medical records of 152 consecutive patients referred to a PH center over a 1-year period of time and who underwent quasi simultaneous (within 1 hr) echocardiography and right heart catheterization. Echocardiography was performed as usually recommended for the assessment of PH and left heart conditions. PH was defined by a mean pulmonary artery pressure (mPAP) > 25 mmHg. Post-capillary PH was diagnosed on the basis of a wedged PAP (PAWP) > 15 mmHg.

Results: Ten percent (17%) had no PH, 81/152 (53%) had pre-capillary PH and 61/152 (40%) had post-capillary PH. The following echocardiographic variables predicted pre-capillary PH: right greater than left heart chambers surface area at end-diastole (p=0.0018), left ventricle eccentricity index ≥ 1.1 (p=0.0039), dilated inferior vena cava (IVC) with no inspiratory collapsibility (p=0.0076), E/e’ ratio > 10 (p=0.0001), right ventricle forming the apex (p=0.0144). E/e’ coefficients from multiple logistic regression were significant for dilated IVC with no inspiratory collapsibility (p=0.0464) and E/e’ > 10 (p=0.0002). A score based on E/e’ coefficients, ranging from 3 to 34 points gave an optimal discrimination at > 5, with a positive predictive value of 88% and a negative predictive value of 78% for pre-capillary PH.

Conclusion: Echocardiography allows for a clinically satisfactory differential diagnosis between pre- and post-capillary PH.

P1367 | BENCH
Pulmonary vascular remodeling in the Fontan circulation

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Purpose: The Fontan circulation is a definitive palliation for patients with a univentricular heart in which systemic venous return flows directly into the pulmonary vascular bed without support of a subpulmonary ventricle. The Fontan circulation is characterized by a gradual attrition over time, that has been contributed to the un-physiologic pre- and afterload of the single ventricle, the chronically increased systemic venous pressures and recently, to chronic non-pulsatile flow in the pulmonary vascular bed. A gradual increase of the pulmonary vascular resistance could be a key factor in the long-term failure of the Fontan circulation, although its mechanism is insufficiently explained. We hypothesized that chronic non-pulsatile flow, present in the Fontan circulation, is associated with adverse pulmonary vascular remodeling in small pulmonary vessels.

Methods: Pulmonary vascular histomorphometric analysis and immunohistochemistry were performed on lung tissue obtained at autopsy from 12 Fontan patients and 24 age-matched controls. The Fontan patients were assigned to a “acute” group A (death < 15 days after the Fontan operation; n=5) or a “chronic” group B (death > 5 years after the Fontan operation; n=7). Two age-matched control groups (n=10 and n=14 respectively) were included.

Results: The intima thickness (p=0.002) is significantly increased and the media (p=0.028) is significantly smaller in intra-acinar pulmonary vessels of the older Fontan patients (n=7) compared with age-matched controls (n=14). The age at death (r=0.964, p<0.001) and the duration of the Fontan circulation (r=0.714; p=0.036) are both significantly positive correlated with intima thickness in the older Fontan group (n=7). Immunohistochemistry showed media attenuation and severe intimal thickening of the intra-acinar pulmonary vessel wall, the composition of this intimal thickening is acellular fibrosis with collagen deposition.

Conclusion: This study shows significant adverse pulmonary vascular remodeling of the intra-acinar pulmonary vessels in the Fontan circulation associated with chronic non-pulsatile flow, consisting of involution of medial smooth muscle.
cells and the presence of eccentric intimal fibrosis with collagen deposition. This pattern of pulmonary vascular remodeling is strikingly different from vascular remodeling known to occur in pulmonary arterial hypertension.

**P1368 | BENCH**  
Apolipoprotein E deficiency is a novel risk factor for pulmonary arterial hypertension (PAH) independently of insulin resistance and dyslipidemia  
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Apolipoprotein E (ApoE) is expressed in and secreted from human pulmonary artery smooth muscle cells (HPASMCG). Downregulation in lungs from PAH patients, and a transcriptional target downstream of bone morphogenetic protein receptor II (BMP-RII), i.e. the receptor that is dysfunctional in many forms of PAH.

**Purpose:** To determine whether normoxic ApoE−/− mice — in the absence of high fat diet and IR — develop PAH, right ventricular hypertrophy and enhanced peripheral pulmonary artery (PA) muscularization with aging.

**Methods and methods:** Male ApoE−/− mice and controls (n=4-8) were fed regular chow for 15 weeks or 1 year. 1.4F catheter was inserted via the jugular vein for assessment of right ventricular systolic pressure (RVSP). Systemic BP, LV fractional shortening and cardiac output (CO) were determined by tail-cuff method and echocardiography. For assessment of right (RVH) and left (LHV) ventricular hypertrophy, we calculated the mass ratios of RV to LV+septum (RV/LV+S), and LHV to LV. PPA muscularization was determined by PA morphometry at alveolar wall level and calculation of the ratio: fully and partially muscularized peripheral PA/total number of peripheral PA. Fasting blood glucose, plasma insulin and adiponectin were measured with a glucometer and RIA. We further investigated the growth-inhibitory effect of recombinant ApoE (10 μg/ml) on PDGF-BB-induced HPASMCG proliferation by cell count and MTT assay, and RV/LV ApoE mRNA expression by qPCR. Statistics: One-way ANOVA/Bonferroni posthoc test.

**Results:** 15 wk old ApoE−/− mice did not differ from controls in terms of RVSP (23.2 ± 20.0 mmHg), RV/LV+S (0.30 ± 0.26), PPA muscularization (8.14 ± 2.32%), CO and BP. However, when compared to age-matched controls, 1yr-old apoe−/− mice developed PAH (RVSP 29.5 ± 22.8 mmHg), RVH (RV/LV+S 0.40 vs. 0.23) and increased PPA muscularization (30.9 ± 11.3%, n=4-10; p < 0.001) in the absence of IR, as indicated by similar glucose, insulin and adiponectin levels. One year old ApoE−/− mice had lower plasma cholesterol and triglyceride levels than their younger counterparts. LV function, LV/BW, CO, BP and HCT were similar at 1 year of age. Preliminary qPCR analysis shows abundant ApoE mRNA expression in the murine RV and LV. Recombinant ApoE protein blocked PDGF-BB-induced proliferation of HPASMCG.

**Conclusions:** ApoE deficiency in itself appears to be a novel risk factor for PAH independently of IR and dyslipidemia.

**P1369 | BENCH**  
Specific targeting of activated platelets allows detection of pulmonary embolism with a single-chain antibody functionalized for MR imaging  
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Introduction: Pulmonary embolism is a major source of morbidity and mortality worldwide. Currently used techniques for the detection of pulmonary embolism, as contrast enhanced computed tomography or nuclear imaging, still bear the challenge of persistent exposure to radiation. However, standard radiation-free angiographic diagnosis of PAH (mean age: 45.9 ± 16.3 years; 72.2% males), of whom 23.3% had associated AoC. First-degree relatives (FDR) underwent a transthoracic echocardiography. This newly developed SRPA technology may help to investigate the mechanism of vascular remodeling associated with PAH.

**Conclusion:** SRPA was useful to visualize micro-vasculature remodeling in PAH. Decreased pulmonary micro-vasculature in PAH was accompanied by decreased pulmonary capillaries detected with IR and echocardiography. This newly developed SRPA technology may help to investigate the mechanism of vascular remodeling associated with PAH.

**Valve disease: Miscellaneous**

**P1372 | BEDSIDE**  
Anatomy, function and family pattern of bicuspid aortic valve: what does the addition of aortic coarctation add?  
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Background: Frequent coexistence of bicuspid aortic valve (BAV) and aortic coarctation (AoC) suggest a common underlying developmental defect. Familial aggregation in both conditions supports the existence of a genetic basis. Our aim was to compare familial aggregation, phenotypic concordance and the prevalence of valvular and aortic complications in individuals with BAV, with AoC and without AoC (BAVNC).

**Methods:** We studied 90 consecutive families of patients with an echocardiographic diagnosis of BAV (mean age: 45.9 ± 16.3 years; 72.2% males), of whom 23.3% had associated AoC. First-degree relatives (FDR) underwent an antero-posterior X-ray to assess the phenotype, function and the presence of asymmetric aortic SA.

**Results:** BAV phenotype in probands was anteroposterior in 75.4% AoC showed a tendency to have BAV without raphe in a higher proportion than BAVNC. In BAV, 0.2% had aortic regurgitation. BAV was significantly more frequent in BAVNC, even after adjusting for age.
sex, body surface and valvular function. One BAVNC patient suffered an aortic dissection. No differences were observed regarding BAV prevalence or opening valve configuration in FDR. Global prevalence of BAV in FDR was 6.5%, higher than in the general population (0.5-1%). BAV phenotype was not constant among probands and FDR, with no differences observed for this discordance between groups (Table).

### Results

Higher TR grade was associated with several clinically significant cardiac abnormalities including LVEF ≤ 45%, moderate or severe mitral regurgitation, RV dysfunction and pulmonary artery systolic pressure (PASP) > 50 mm Hg (All P < 0.001). The median PASP was 38, 47, 55 and 60 mm Hg in patients with none/trivial, mild, moderate and severe TR, respectively (P < 0.001). There was a graded increase in the number of signs of congestion with increasing TR severity (P < 0.001). In addition, higher TR grade was associated with higher BNP, worse renal function and abnormal liver function tests.

Kaplan-Meier analysis showed a graded increased probability of mortality during follow up with increasing TR severity (Fig. 1). However, in a multivariable Cox model adjusting for clinical and echocardiographic parameters, TR was not associated with increased mortality risk. Compared with patients with none/trivial TR, the adjusted hazard ratio for mortality was 1.04 (95% CI 0.71–1.52), 1.32 (95% CI 0.85–2.06) and 1.44 (95% CI 0.85–2.06) in patients with mild, moderate and severe TR, respectively.

### Conclusion

The prevalence of BAV was similar in FDR of patients with and without AoC, although a high percentage of phenotypic discordance was found within the same family. The population with isolated BAV had higher rates of AA dilation, valve degeneration and aortic regurgitation compared to that combined with BAV and AoC.

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**P1373 | BENCH**

### The content of CD14++CD16+ monocytes and the extent of monocyte activation before TAVI is associated with death after TAVI

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#### Purpose

A systemic inflammatory syndrome (SIRS) often occurs after TAVI and is known to be a strong predictor of mortality. Mechanism for initiating SIRS after TAVI are not yet known. The proinflammatory CD14++CD16+ monocyte subset has been associated with cardiovascular events and death in patients with chronic kidney disease. As these monocytes with a CD14++CD16+ phenotype are known to be active producers of inflammatory cytokines, like TNFα, we hypothesize that the level of these monocyte subset has an impact on the development of inflammatory reactions after TAVI. Further, we hypothesize that the content of CD14++CD16+ monocytes and the extend of activation of monocytes overall predict a worse outcome after TAVI.

#### Methods

102 patients (mean age: 81.6±5.4 years) with symptomatic severe aortic stenosis underwent TAVI with a transfemoral approach. In all patients Flow-cytometric quantification analyses of peripheral blood were done on the day before the procedure and on day 1 and day 7 after TAVI. The content of “proinflammatory” monocytes were detected by co-expression of the monocyte specific lipopolysaccharide receptor CD14 and the FcγRIII receptor CD16. The extend of activation of monocytes was determined by quantification of the cell adhesion molecule MAC-1 (CD11b). Additionally, proinflammatory cytokines such as C-reactive protein (CRP) were measured at baseline and the days after TAVI.

Results: Initial patients received TAVI successfully. 3 months after TAVI 15 patients of all 102 patients died, predominantly without a dysfunction of the implanted aortic valve. No differences in EURO-Score, comorbidities like diabetes, obesity, hypertension and CAD were found between survivors and patients who died during follow up. A high content of CD14++CD16+ monocytes before TAVI (13.8% vs. 8.4%, p < 0.001) and on day one after TAVI (18.8% vs. 10.5%, p = 0.01) was independently associated with death at 3 months after TAVI. A high expression of CD11b on all monocytes before TAVI and the absolute number of CD14++CD16+ monocytes before TAVI, but not of CD14+CD16- monocytes were associated with an increase of CRP (p < 0.001), in the first two days after TAVI.

Conclusions: The number of CD14++CD16+ monocytes and the extent of monocyte activation before TAVI is independently associated with death in the intermediate follow up period after TAVI. These cells may act as initiators of systemic inflammatory processes shortly after TAVI.

**P1374 | BEDSIDE**

### Tricuspid regurgitation and clinical outcomes in patients with heart failure


#### Background

Hemodynamically significant tricuspid regurgitation (TR) is common in patients with heart failure (HF) and has been reported to portend poor prognosis. However, it is still unknown whether TR is a surrogate marker of advanced myocardial and valvular heart disease or a mediator of disease progression.

#### Methods

We studied 542 patients admitted for HF. TR severity was assessed by all echocardiographic criteria. We excluded patients with severe TR due to right heart failure with acute RV dilation. We followed the patients up for 2 years.

#### Results

Severe TR (regardless of etiology), as defined by ≥ 21 mm/m², was observed in 115 (21.3%) patients. The median age was 64 years (range 25–94) and 248 (45.8%) were males. Severe TR was associated with a mortality rate of 57.5% at 2 years (95% CI 49.9–64.9%). Severe TR was associated with several clinical and echocardiographic parameters as compared to none/trivial TR (Table). Severe TR was the strongest predictor of mortality (HR 2.99, 95% CI 2.17–4.13) among all variables (Tables). A high content of CD14++CD16+ monocytes before TAVI and the absolute number of CD14++CD16+ monocytes were associated with an increased mortality risk. Compared with patients with none/trivial TR, the adjusted hazard ratio for mortality was 1.04 (95% CI 0.71–1.52), 1.32 (95% CI 0.85–2.06) and 1.44 (95% CI 0.85–2.06) in patients with mild, moderate and severe TR, respectively.

#### Conclusion

In patients with HF, the association between TR and mortality can be explained by associated co-morbidities.

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**P1375 | SPOTLIGHT**

### The value of D-dimer in predicting prosthetic valve thrombosis in patient undergoing valve surgery

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#### Purpose

Nowadays, plasma D-dimer level has been considered to be a diagnostic marker for predicting cardiac thrombotic events appearance, the goal of this prospective study was to investigate the diagnostic value of plasma D-dimer levels in predicting prosthetic valve thrombus (PVT).

#### Methods

The study group comprised 95 consecutive patients (59 women and 36 men; mean age, 44.3±11.6 years) with prosthetic heart valves that were referred for surgery.
to our echocardiography laboratory from after prosthetic valve surgery. D-dimer levels were determined by quantitative D-dimer, micro-latex immunassay.

Results: Transesophageal echocardiography demonstrated the presence of a distinct mobile echo interpreted as a local thrombus on the atrial surface of the mitral prosthesis in 47 asymptomatic patients (32 patients with MVR, 21 patients with AVR, and 10 patients with AVR + MVR). Analysis of variance also revealed a higher plasma D-dimer level in PVT group compared with non-PVT group (1378.79±181.54 μg/l vs. 369.52±181.42 μg/l, p<0.001). Multiple linear regression analysis identified D-dimer levels as the significant independent factor for PVT formation (OR = 1.011, P<0.001). According to the ROC curve analysis, plasma D-dimer level had a high value for discriminat- ing PVT non-PVT condition (c = 0.951, 95% CI = 0.901 – 0.999). A cutoff D-dimer value of 890 μg/l was determined for discriminating between the patient with and without PVT, yielding a sensitivity of 89.9% and a specificity of 97.9%.

Conclusion: High plasma D-dimer levels were identified as a predictive marker of thromboembolic events in patients with prosthetic valves.

P1379 | BEDSIDE Evaluation of direct current cardioversion following percutaneous transmitral commissurotomy in rheumatic mitral stenosis patients with atrial fibrillation for maintaining long term sinus rhythm

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Purpose: In patients with rheumatic mitral stenosis (MS), atrial fibrillation (AF) is associated with unfavourable prognosis. High risk of thromboembolism renders restoration of sinus rhythm (SR) a preferred strategy over rate control. Percutaneous transvenous mitral commissurotomy (PTMC) is effective in improving left ventricular function and may shorten hospital stay. However, results with restoration of SR remain limited.

Methods: Prospective randomized study aimed at evaluating efficacy of cardioversion for rhythm control in patients with long standing AF in rheumatic MS, after successful PTMC. Primary endpoint was maintenance of SR after 09 months. Secondary endpoints were functional capacity, embolic episodes, drug side effects and mortality.

Results: Thirty five patients were studied in 02 groups -Group 1 (n=20) only PTMC, Group 2 (n=15) PTMC + Direct Current cardioversion (DCC) + Amiodarone for 06 weeks. In group 2 all patients had successful cardioversion to SR. At the end of follow up (09-13 months), 95% in group 1 were in AF, while 5% re-verted to SR spontaneously. In Group 02, 87% patients were in SR and 13% had reverted to AF. Difference in rate of SR was 0.82 (95% CI 0.2, 1.01) (p<0.001), with a relative risk of 1.95, 95% CI P=0.001 for patients to be in AF who undergo PTMC. There was significant improvement in quality of life (SF36) score in group 2 (p=0.001-0.004), with no deaths, stroke or adverse drug effects in either group.

Conclusion: In patients with rheumatic MS and AF, DCC following successful PTMC, may be a reasonable strategy to attain long term SR.
LAA ejection fraction was measured using the modified Simpson’s method.

Results: The mean age of the 56 enrolled patients was 36.4±7 years. 45% were in sinus rhythm. PMC was successful in all patients. The pulse Doppler velocities of the LAA were measured, including peak early diastolic (E wave), peak late diastolic (A wave), and peak systolic (S wave). The corresponding tissue Doppler velocities of the LAA, including peak early diastolic (E(LAA)), peak late diastolic (A(LAA)), and peak systolic (S(LAA)), were also measured. LAA ejection fraction was measured as a dimensionless ratio of diastolic transmitral stroke distance to diastolic transmitral valve orifice area. In controls optimal VFT was found to be 7.8±1.8 and was proportionately higher with increasing severity of mitral stenosis (Table 1).

Conclusion: LV VFT was suboptimal with MS. It becomes more out-of-range with increasing severity of MS and correlate with increasing LA size and worsening emptying function. LA emptying function and degree of mitral valve opening appears to be determinants of LV flow propagation.
ameters (20.7 vs. 20.1 mm; p < 0.001). SVI was also higher in the group of distal LVOT diameter than in the proximal LVOT (41.6 vs. 39.4 ml/m²; p < 0.001). There was a strong correlation between both SVI (r = 0.881; p < 0.001), however when we classified the patients according to the flow, there was a higher proportion of LF patients in the proximal LVOT group (24.7 vs. 16.9%; p < 0.001), with discrepancies in the classification of 10% of the patients. No differences were found in the percentage of patients with LF according to age (older or younger than 50 years) in both measurements and nor according to gender in the distal LVOT group. Nonetheless, there was a higher proportion of LF in male patients in the proximal LVOT group (27.0 vs. 9.6%; p < 0.044).

Conclusions: Carefully evaluation of LVOT diameter is crucial in the evaluation of SV and AV area. Both methods of measurement provide significant differences in the LVOT diameters, with a larger distal LVOT diameter. These differences are translated into a higher SV and a different proportion of LF patients when using the distal LVOT diameter.

P1386 | BEDSIDE
Prognostic value of tricuspid annular dilatation assessed by three-dimensional transesophageal echocardiography

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Background: This study aimed to evaluate the relationship between tricuspid annular dilatation (TAD) and tricuspid regurgitation (TR), and the prognostic value of TAD using three-dimensional transesophageal echocardiography (3D TEE).

Methods: Tricuspid annular area (TAA) was measured in 116 patients using 3D TEE. Patients were classified into three groups based on TAD measurement in A4C (n=77), moderate TR (n=26, severe TR (n=13). Moreover, patients were classified into two groups based on rehospitalization for heart failure (HF): HF (+) group (n=18) and HF (-) group (n=98).

Results: TAA in the severe TR group was significantly larger than that in the mild and moderate TR groups (18.4 ± 3.8 cm² vs. 11.7 ± 3.2 cm², 12.3 ± 3.4 cm², p < 0.05). TAA in the HF (+) group was significantly larger than that in the HF (-) group (16.8 ± 4.3 cm² vs. 11.8 ± 3.3 cm², p < 0.001). In receiver operating characteristics curve assessing the ability of TAA to predict hospitalization for HF, the area under the curve was 0.84. TAA ≥ 15 cm² predicted hospitalization for HF with 77.8% sensitivity and 84.6% specificity. The incidence of hospitalization for HF during 3 years was significantly higher in the TAD (+) group (TAA ≥ 15 cm²) than the TAD (-) group (48.3% vs 4.6%, p < 0.001, Figure).

Conclusions: The results of this study suggested a possible association between TAD and the TR severity. TAD estimated using 3D TEE may predict hospitalization for prospective HF.

P1387 | BEDSIDE
Evaluation of the tricuspid annulus size: clinical implications from comparison between 2D-transthoracic and 3D-transesophageal echocardiography


Background: Tricuspid annuloplasty is recommended during left-heart valve surgery when tricuspid annulus (TA) is dilated, independently of the degree of tricuspid regurgitation, but the methodology to measure TA and thresholds are not clearly defined. We aimed to compare TA diameter (TAD) measurements performed using bi-dimensional transthoracic echocardiography (2D-TTE) in the 4 different views to three-dimensional measurements performed during transesophageal echocardiography (3D-TEE) and to define thresholds of TA enlargement for routine practice.

Methods: 2D-TTE measurement of the TAD was performed in parasternal long-axis view of the right ventricle inflow, parasternal short-axis, apical 4-chamber (A4C) and sub-costal views in 184 prospectively enrolled patients and 66 healthy volunteers. 3D dynamic volumetric data of the TA were also acquired by TEE using a matrix array transducer (X7-2T, Philips) in the 184 patients. Multplanar reconstructions were performed offline using dedicated software (QLab7, Philips) to measure the long-axis (LA) of the TA.

Results: In the 184 patients, TAD measurements were not different between the 4 TTE views (P>0.13), but A4C was the most feasible and the most reproducible method (Table). TAD measurement in A4C view by TTE (3.9 ± 0.62 cm²) was well correlated (r = 0.84, p < 0.0001) to LA by 3D-TEE (4.3±0.63 cm²), but with a systematic 4mm underestimation. In the healthy volunteers, mean value of TAD in A4C was 3.2±0.4 cm² and 1.8±0.23 cm² and the upper limit of 95% confidence interval was 4.2 cm² or 2.3 cm².

Tricuspid annulus diameter by 2D-TTE

2D-TTE views

<table>
<thead>
<tr>
<th>TA diameters measurements (cm)</th>
<th>Feasibility (%)</th>
<th>Reproducibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasternal long-axis view of the right ventricle inflow</td>
<td>3.77 ± 0.53</td>
<td>76</td>
</tr>
<tr>
<td>Parasternal short-axis</td>
<td>3.80 ± 0.56</td>
<td>65</td>
</tr>
<tr>
<td>Apical 4-chamber</td>
<td>3.90 ± 0.62</td>
<td>92</td>
</tr>
<tr>
<td>Sub-costal</td>
<td>3.86 ± 0.61</td>
<td>73</td>
</tr>
</tbody>
</table>

Conclusion: TAD measurement in A4C view by 2D-TTE was highly feasible, reproducible and accurately reflected TA size, even if it was systematically underestimated. In healthy volunteers, 3D-TEE was non-reproducible and accurately reflected TA size, even if it was systematically underestimated.

P1388 | BEDSIDE
Leaflet adaptation as a determinant of tricuspid regurgitation severity in patients with pulmonary hypertension

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Purpose: Tricuspid regurgitation (TR) is a risk factor for mortality and morbidity in pulmonary hypertension (PH). TR severity varies among patients with comparable degrees of PH right ventricular (RV) remodeling. The contribution of tricuspid leaflet adaptation to the pathophysiology of functional TR has yet to be examined. We hypothesized that tricuspid leaflet growth occurs in PH, and that its adequacy relative to RV remodeling is a determinant of TR severity.

Methods: A prospective cohort of 255 patients with PH from pre- and post-capillary etiologies was assembled at two hospitals. Those with pacemakers or organic or TR were excluded. Patients underwent a 3D-echochography focused on the tricuspid apparatus. TR severity was quantified by the vena contracta. Tricuspid leaflet area was traced by blinded readers using the Omni 4D custom software package. Tricuspid closure area, a measure of annulus area and tethering, was similarly traced. The ratio of leaflet area to closure area was calculated, reflecting the adaptation (i.e. growth) of the valve leaflets to occlude the closure area and thus maintain valvular competency. Regression and ROC analyses were employed to test the effect of leaflet-to-closure area on TR severity.

Results: Functional TR was mild in 116 (45.5%), moderate in 86 (33.7%), and severe in 53 (20.8%). PH patients had a twofold increase in RV volumes, 70% increase in annular area, and 47% increase in leaflet area compared with normal controls. Those with severe TR had an inadequate increase in leaflet area relative to closure area, such that the ratio of leaflet-to-closure area < 1.8 was highly predictive of severe TR (odds ratio 68.7; 95% CI 16.2, 292.7). Leaflet area and closure area demonstrated additive effects in predicting TR severity: the median vena contracta was 8.5 mm in the group with small leaflet area and large closure area (N=48), 4.8 mm in the group with small leaflet area and large closure area (N=85), 3.3 mm in the group with small leaflet area and small closure area (N=76), and 3.0 mm in the group with large leaflet area and small closure area (N=6).

Conclusions: Leaflet adaptation plays a significant role in defining which PH patients are affected by severe functional TR. The ratio of leaflet-to-closure area is a powerful indicator of TR severity that reflects the adequacy of leaflet adaptation relative to RV remodeling. The therapeutic impact of these findings may be to guide surgical repair of functional TR by identifying which patients stand to benefit from a tricuspid leaflet augmentation strategy.

P1389 | BEDSIDE
Accuracy of two- and three-dimensional echocardiography to diagnose congenitally bicuspid aortic valves: a surgical pathology validation study

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Background: Bicuspid aortic valve (BAV) is the most common congenital heart valve abnormality, which often leads to severe aortic stenosis (AS) or insufficiency (AR) and ascending aorta dilatation. Preoperative recognition of BAV, commonly by echocardiography, is crucial to properly select and plan therapeutic proce-
dures. However, the relative accuracy of two (2DTEE) and three-dimensional (3DTEE) transoesophageal echocardiography in diagnosing BAV remains to be clarified.

**Methods:** Single center, prospective study. From January to May 2013, 40 consecutive patents (37 years, range 19-82 years; 53% males) had aortic valve surgery at our Institution. 18 (45%) AS; 8 (20%) pure AR; and 14 (35%) combined AS and AR. All patients underwent 2DTEE and 3DTEE in the operating room to assess aortic valve morphology before surgery. All echocardiograms were reviewed blindly by the same investigator, and the aortic valve morphology was categorized as bicuspid, tricuspid, or indeterminate. Echo findings were compared with surgical pathology analysis (gold standard) (Table). Sensitivity, specificity, negative (NPV) and positive (PPV) predictive value of 2DTEE and 3DTEE were calculated.

**Results:** Compared with surgical pathology analysis, 3DTEE (Sens=100%; Spec=96%; NPV=100%; PPV=93%) was significantly more accurate than 2DTEE (Sens=36%; Spec=100%; NPV=75%; PPV=100%) in the overall study population (Table). In the subgroup of 8 patients with isolated AR, 3DTEE and 2DTEE showed similar accuracy (Sens 100%, Spec 98%, NPV= 100%, PPV= 98%).

<table>
<thead>
<tr>
<th>Surgical pathology analysis (n=40)</th>
<th>3DTEE+ (n=14)</th>
<th>3DTEE− (n=26)</th>
<th>2DTEE+ (n=5)</th>
<th>2DTEE− (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAIV+</td>
<td>13</td>
<td>1</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td>BAIV−</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>2DTEE+</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2DTEE−</td>
<td>9</td>
<td>26</td>
<td>0</td>
<td>26</td>
</tr>
</tbody>
</table>

**Conclusions:** When compared with gold standard pathological anatomy, 3DTEE proved to be a highly accurate imaging technique for the diagnosis of BAV. In pts with AS, the possibility to visualize the valve from the aortic perspective by 3DTEE adds significant diagnostic value in comparison with standard 2DTEE.

**P1390 | BEDSIDE**

Three-dimensional changes of the mitral annulus geometry and dynamics in patients with functional mitral regurgitation: insights for medical valve repair

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**Background:** Current three-dimensional transthoracic echo (3DTEE) allows quantitative assessment of mitral annulus (MA) geometry and function comparable with transoesophageal approach.

**Objectives:** To provide better insights into the pathophysiology of functional mitral regurgitation (FMR) using 3DTEE.

**Methods:** 56 pts with mild to severe FMR due to ischemic cardiomyopathy (58±17 yrs, 42 men) and 52 age- and gender-matched controls (C) underwent 3D full-volume acquisition of the mitral valve (MV). MA geometry was analyzed using prototype software package (MV assessment 2.3, TomTec, D). MA parameters were recorded at 4 reference frames: mitral valve closure (MVC), mid- and end-systole, and the frame of minimum value. Time from MVC to minimum value was recorded as % of systole duration.

**Results:** FMR pts presented larger antero-posterior (AP) and anterolateral-postero medial (ALPM) diameters, MA area (MAA) and circumference (MAC) at every reference frame (*p<0.001) (Figure). FMR pts also showed higher MA sphericity index (SI), MV tenting volume and area at every reference frame (*p<0.001). MA was flatter over the entire systole in FMR than in C (*p<0.001). In addition, FMR patients presented longer time to maximum MA contraction, to minimum AP (26±24% vs 11±9%) and ALPM diameters (26±24% vs 13±8%), to minimum MAA (20±16% vs 11±8%) and MAC (21±17 vs 11±6%), and to minimum SI (41±28% vs 20±18%) (*p<0.001). MAA fractional change (15±5% vs 28±5%) and MA displacement (5±3 vs 10±2 mm) were lower in FMR than in C (*p<0.001).

**Conclusion:** Quantitative analysis revealed altered MA geometry and dynamics in pts with FMR. Reduced and delayed MA conformational changes might explain the early occurrence of regurgitation in FMR. Our findings may be useful for planning future procedures for MV repair.

**P1391 | BEDSIDE**

Incremental utility of live real time three dimensional transthoracic echocardiography in the assessment of morphological abnormalities of the mitral valve in rheumatic heart disease

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**Purpose:** Live real time three dimensional (RT 3D) transthoracic echocardiography (TTE) was employed to objectively assess the morphological abnormalities of mitral valve associated with rheumatic heart disease (RHD) with a view to assess the limitations of two dimensional (2D) TTE, if any, in visualizing these abnormalities.

**Methods:** The patient group comprised of 31 adult cases of clinically diagnosed RHD and the echocardiographic studies were performed using Philips I E33 ultra sound system (Andover USA) by a single, experienced cardiologist. The diagnosis of definite RHD was made on the basis of the World Heart Federation criteria [1].

**Results:** Definite RHD with mitral valve involvement was confirmed by 2D TTE for all the cases. Analysis of the morphological abnormalities of the mitral valve by RT 3D TTE yielded additional following details:

- Cases of pure mitral regurgitation (MR) had greater irregularity of leaflet thickening whereas cases of mitral stenosis (MS) with or without MR had more uniformly thickened valves.
- Prolapse of the middle scallop of anterior mitral leaflet (AML) was visualized in most (25 of 31) cases; additionally prolapse of lateral scallop of AML was seen in 1 case and flail AML with, improper co-aptation of the middle scallop was visualized in 1 case.
- Diastolic doming of the middle scallop of AML into LV was visualized for a minority of cases of pure MR (2 out of 8) whereas it was visualized for almost all the cases of MS (21 of 23).
-Leaflet redundancy and chordal lengthening was not visualized for any case.
- Chordal thickening and shortening was not detected for any case of pure MR but it was visualized for all the cases of MS.

**Conclusions:** The irregular thickening of mitral leaflets potentially contributes to severity of MR. Uniform thickening found associated with MS is less often co-existant with MR. Prolapse of the AML is the most consistent and pathognomonic morphological abnormality of RHD which can be readily differentiated by RT 3D TTE from myxomatous degeneration. This can be detected by 2D TTE and thus be included in diagnostic criteria. Irregular leaflet thickening can be easily missed by 2D TTE, especially in cases of pure MR which perhaps represent early stages of disease. Therefore, exclusion of AML prolapse and inclusion of leaflet thickening potentially compromises the specificity and sensitivity of the WHF criteria [1].

**Reference:**

**P1392 | BEDSIDE**

Prevalence of valvular strands during routine echocardiographic examinations

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**Purpose:** Valvular strands [Lambl’s excrescences], have been associated with...
increased embolic risk. In previous studies valvular strands have been detected by trans-esophageal echo. The current high resolution echocardiographic systems allow detection of valvular strands [Lamb's excrescences] often even by transesophageal echocardiography.

We sought to assess incidence of valvular strands [Lamb's excrescences] during routine trans-thoracic and/or trans-esophageal echocardiography and define their relation to the cardiovascular risk factors, co-morbidities and outcome.

Methods: Over 21000 echocardiographic examinations were performed at our hospital during 2008-2012 and were searched for reporting of valvular strands [Lamb's excrescences]. 150 such studies were identified and the presence of valvular strands [Lamb's excrescences] was confirmed. Clinical characteristics of these patients, co-morbidities and outcome were analyzed and compared with the same parameters of 150 age and gender matched individuals without valvular strands.

Results: Incidence of valvular strands was maximal at age 61-70 [0.94%], occurred more common in men than in women, 92 versus 58, p < 0.00001. Valvular strands were more common on aortic than on mitral valve 125 versus 36 respectively, p < 0.00001, were more often associated with thickened or calcified valve, and predominantly occupied ventricular portion of aortic valve and atrial portion of the mitral valve, p < 0.00001. Valvular strands were not associated with mortality, but were more frequent in patients with an embolic event 40 versus 20, p < 0.005.

Conclusions: Valvular strands [Lamb's excrescences] appear not to affect life expectancy, but are associated with embolic/cerebrovascular risk, are more common in older patients, in men than in women, and are more commonly located on the aortic than on mitral valve.

P1393 | BEDSIDE
Cardiovascular outcome predictors in systemic sclerosis
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Background: Cardiovascular (CV) involvement is recognized as a poor prognostic factor in systemic sclerosis (SSc). The aim of this study was to evaluate the usefulness of nailfold video-capillaroscopy (NVC), brain natriuretic peptide (BNP) blood level and exercise echocardiography to predict the occurrence of CV events in SSc.

Methods: We prospectively enrolled 65 patients with SSc (age 54±14 years, 30% female). All patients underwent a graded semi-supine exercise echocardiography. Baseline resting pulmonary hypertension (PH) and PH during follow-up (FUPH) were defined as systolic pulmonary arterial pressure (sPAP) ≥ 35 mmHg, and exercise-induced PH (EIPH) as sPAP≥ 50mmHg during exercise.

Results: EIPH was present in 21 patients. During FU (27±18 months), 13 patients developed FUPH and 9 presented CV complications (2 transient ischemic attacks, 2 peripheral vascular complications, 22.4% had a 72.5% sensibility and 68.6% specificity for predicting residual L VH at 6 months; AUC 0.732, p<0.001). Baseline sPAP levels tended to be higher in women (775.7±250.2 vs 649.1±94.1 ng/ml; p=0.067) and TIMP1/MMP1 levels positively correlated with baseline LVM index (r=0.681, p=0.003) only in women. Moreover, women had significantly more fibrosis than men (median of 15.39% [P25-75:7.95-20.99] vs 10.04% [P25-75:6.00-14.96]). In higher TIMP2 and TIMP1/MMP1 levels correlated with lesser 6 month LVM regression (r=0.260, p=0.022, TIMP1/MMP1=r=0.7-0.748, p<0.005). In AS women had more inappropriate LVEF than men and have more residual hypertension after surgery. A gender-specific ECM remodeling, with more interstitial fibrosis in women, could explain these differences.

TAVI: REGISTRIES AND OUTCOMES

P1396 | BEDSIDE
Transaortic transcatheter aortic valve implantation - experience from the first multicenter, multinationsal prospective registry (ROUTE)
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Objective: Transaortic transcatheter aortic valve implantation (TAO-TAVI) is an alternative access route for patients with significant respiratory disease, poor left ventricular function, chest wall deformities and after multiple redo surgeries. ROUTE is the first multicenter, multinational prospective registry to document the course and outcomes of patients undergoing this new procedure.

Methods: ROUTE commenced in February 2013 and aims to document TAO-TAVI implantation up to 25 sites across Europe with about 200 patients included. The principal research objective is to determine overall mortality rates within 30 days after TAVI. Secondary objectives relate to TAVI related mortality, VARC complications and to identify predictors of adverse outcomes.

Results: As of February 2016 a total of 83 patients undergoing TAO-TAVI had been included: 68.1% would also have been eligible for the TA and 22.2% for the TF approach. The principal reason for choosing TAO was that it was the standard procedure at the site (49.3%), followed by an adverse vessel status (21.3%). Patients had a mean age of 82.1±6.3 years, 53.0% were female and 14.8% were smokers. Mean STS risk score was 11.1±7.6 and the peak transvalvular gradient 70.7±21.1 mmHg. The majority of patients had NYHA class III/IV heart failure (84.7%).

Ministernotomy was the default access route (100%). The procedure was completely transapical in a mean of 118.3±36.6 min and 14.6±7.3 min of fluoroscopy. Most received a 26 mm valve (44.7%), followed by 29 mm (29.0%) and 23 mm (26.3%). Overall 97.4% of valves were successfully deployed and 2.6% received a second valve (in valve). One patient was converted to conventional surgery. There were no perioperative deaths, no aortic root 1 tearing, no valve embolization, no strokes, no ventricular arrhythmias, no pericardial & pleural effusion, no bleeding complications.

Conclusion: TAVI in patients with poor operative risk and significant respiratory disease is a feasible and safe option for inoperable or high risk patients. Low implantation (over 8mm) has been frequently implicated with moderate or severe paravalvular aortic regurgitation (PVR). However, it has not been evaluated the effect of high implantation on the outcome of this procedure. The purpose of this study is to assess whether high implantation affects the short- and long-term outcome of the procedure.

Methods: Consecutive patients who underwent TAVI were evaluated. Echocardiographic parameters were recorded before the procedure, at discharge of the procedure and at postdischarge.

P1397 | BEDSIDE
Impact of “high” implantation of self-expandable valve in both short- and long-term outcome of patients undergoing TAVI
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Objective: Transcatheter aortic valve implantation (TAVI) is an emerging treatment option for inoperable or high risk patients. Low implantation (over 8mm) has been frequently implicated with moderate or severe paravalvular aortic regurgitation (PVR). However, it has not been evaluated the effect of high implantation on the outcome of this procedure. The purpose of this study is to assess whether high implantation affects the short- and long-term outcome of the procedure.

Methods: Consecutive patients who underwent TAVI were evaluated. Echocardiographic parameters were recorded before the procedure, at discharge of the procedure and at postdischarge.
Impact of access on TAVI procedural and midterm term follow up: a meta-analysis of 13 studies and 10468 patients

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Purpose: In most of the patients, Transcatheter Aortic Valve Implantation (TAVI) may be performed using transfemoral (TF) or transapical (TA) approach: however impact of access choice on periprocedural and midterm mid-results remains to be defined. Aim of our study was to evaluate the impact of access choice on short and midterm follow-up after TAVI

Methods: Medline and Cochrane Library were searched for articles describing differences in baseline, peri-procedural and midterm outcomes among patients undergoing TF or TA TAVI. The primary end-point was all-cause mortality at midterm follow-up, while secondary ones were 30 days mortality and in-hospital complications (bleeding and cerebrovascular events). The independent impact of access choice was evaluated with pooled analysis using a random-effect model.

Results: 13 studies with 10468 patients were included. TF was the most exploited strategy (69.5% vs. 30.5%). After adjusting for confounding variables, 30 days and follow-up mortality (median 365 days, range 222-400) were lower in TF patients (p=0.01 [0.88-0.99]) and 1 years mortality (p=0.001 [0.92-0.97], respectively). Regarding periprocedural outcomes, TF reduced risk of bleedings and strokes (OR respectively of 0.74 [0.66-0.82], 0.96 [0.89-0.99] and 0.91 [0.83-0.99] and 0.86 respectively.

Conclusions: TF approach reduces mortality in TAVI patients, due to lower rates of periprocedural bleedings and strokes.
all-cause mortality for STT compared to STS was of 31% (p<0.001), and of 14% (p<0.001) for all-cause mortality at follow up.

Conclusions: STT represents an easy and accurate score to define risk of 30 days and of mid-term mortality for patients undergoing TAVI, improving STS score performance.

P1402 | BEDSIDE
Long-term performance of a nonmetallic, retrievable and repositionable aortic valve in patients with severe aortic stenosis, 5 Year Follow-Up of the 22 F Direct Flow Medical Valve

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Background: There is limited information on 5-year outcome of patients undergoing trans-catheter aortic valve implantation. In particular, long-term results of a non-metallic inflatable valve design has never been reported. Less radial force of this device may impact its stability and hemodynamic function over time.

Aim of the study: To evaluate the 5-year clinical and echocardiographic outcome of the retrievable and repositionable first generation 22F-DFM valve.

Methods and results: From 2007 to 2008 31 symptomatic high-risk for surgery patients (mean age 82±4y) with severe aortic stenosis and a mean logistic EuroSCORE of 29±7 were the subject of this analysis. Clinical, echocardiographic and hemodynamic follow-up were obtained during 5 years. Survival rates were 81%, 69%, 60%, 54% and 54% at 1,2,3,4, 5 years, respectively. At 5 years, all surviving patients were in NYHA-class I. Echocardiography revealed a significant decrease of the mean gradient from baseline (49.1±13.8 mmHg) to 30 days (19.1±6.6 mmHg, p<0.001), which remained stable over 5 years (15.3±6.0 mmHg) (p=NS), At 5-year follow-up aortic regurgitation assessed by TTE was non or trace in all patients.

Conclusions: In this preliminary series, the first generation of the nonmetallic, repositionable and retrievable 22F-DFM valve was associated with acceptable clinical outcome and stable hemodynamic performance over 5 years with trace or less aortic regurgitation in all patients.

P1403 | BEDSIDE
Trends in trans-catheter aortic valve implantation between 2011 and 2012. Results from the GARY Registry

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Background: Trans-catheter aortic valve implantation (TAVI), either by a surgical access (S-TAVI) or by a percutaneous trans-vascular access (V-TAVI), has established as a routine treatment modality for older surgical high-risk patients suffering from severe aortic stenosis. Little is known on current trends concerning patient selection as well as results in the last years.

Methods: We analysed all patients treated with TAVI between 2011 and 2012, who were included in the prospective German aortic valve replacement registry (GARY).

Results: Out of all documented aortic valve replacement therapies (also the surgical ones) the proportion of the TAVI procedures in GARY was 27.6% in 2011 (3938/14247) and 31.9% (5333/16722) in 2012 (p-value: <0.001).

P1404 | BEDSIDE
When and why do patients die after successful transcatheter aortic valve replacement (TAVI)?

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Background: Transcatheter aortic valve replacement (TAVI) is a valuable alternative for patients suffering from severe aortic stenosis and who are not candidates for surgical valve replacement. The overall rate of death in this patient population is reported to be 34% over 24 months.

Aim: The aim of this retrospective analysis was to assess the overall long term mortality and the cause of death in patients after successful TAVI during four years follow-up.

Methods and results: Since 2007 327 TAVI procedures have been performed in our institution (210 transfemoral, 97 transapikal, 20 transaortai). The overall perioperative mortality was 4.9%. The mean annual mortality after successful TAVI was 16.75% TF, 28.57% TA and 11.76% TAO (p<0.05).

The reasons for mortality after the perioperative period comprised cardiac (25.4%), infectious (30.2%), malignancy (9.5%) cerebrovascular (12.7%) bleeding (1.6%) and other reasons (20.6%). There was no significant difference between the different access routes and the causes of death observed. An overview of the timing and the causes of death are given in the graph.

P1405 | BEDSIDE
Mortality prediction using five different risk scores for cardiac surgery in patients undergoing transcatheter aortic valve implantation (TAVI): a multicenter Brazilian registry

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Background: Transcatheter aortic valve implantation (TAVI) has been established as a standard treatment in inoperable patients and an attractive alternative for surgical high-risk patients with symptomatic severe aortic stenosis. Predicting mortality in patients undergoing TAVI is still a challenge. The aim of this study was to evaluate the performance of five risk scores for cardiac surgery on predicting 30- and 30-day mortality among patients of the Brazilian Registry of TAVI.

Methods: The Brazilian Multicenter Registry prospectively enrolled 418 patients undergoing TAVI in 18 centers between 2008 and 2013. For all patients, the 30-day mortality was calculated using the following surgical risk scores: logistic EuroSCORE I (ESI), EuroSCORE II (ESII), STS Score (STS), Amblor Score (AS) and Guaragna Score (GS). The performance of the risk scores was evaluated in terms of their calibration ( Hosmer-Lemeshow test) and discrimination [area under the receiver-operating characteristic curve (AUC)]

Results: Mean age was 81.5±7.7 years. The CoreValve (Medtronic) was used in 86.1% of the cohort and transfemoral approach was used in 96.2%. The observed 30-day mortality was 9.1%. The mean 30-day mortality predicted by the scores was: ESI, 20.2±13.8%; ESI I, 6.5±13.8%; STS, 17.4±4.4%; AS, 7.0±3.8%; GS, 17.3±10.8%. By using the AUCs, none of the tested scores was able to accurately predict 30-day mortality. The AUC for the scores were: 0.57 (CI 95%: 0.48-0.66; p=0.11) for the ESI; 0.52 (CI 95%: 0.43-0.62; p=0.63) for the ESI I; 0.55 (CI 95%: 0.46-0.64; p=0.26) for the AS; 0.48 (CI 95%: 0.4-0.57; p=0.71) for the STS and
0.54 (CI 95%: 0.45-0.63; p=0.38) for the GS. The Hosmer-Lemeshow test indicated acceptable calibration for all scores (p=0.05).

**Conclusions:** In this real world Brazilian registry, the surgical risk scores were inaccurate in predicting mortality after TAVI. Risk models specifically developed for TAVI are necessary to accurate estimation of patient prognosis.

**MORE ON TAVI**

**P1407 | BEDSIDE**

**Late outcome up to 6 years after transcatheter aortic valve implantation (TAVI)**


**Purpose:** Few data exist on long-term results of TAVI and they are crucial for decision making. We assessed late outcome after transcatheter aortic valve implantation (TAVI), up to 6 years and analysed its predictive factors with a particular emphasis on functional status.

**Methods:** Between October 2006 and December 2009, 123 consecutive patients were discharged alive after TAVI in our institution. Mean age was 82±8 years and 88% of patients were highly symptomatic in New York Heart Association (NYHA) class III-IV. Mean logistic EuroSCORE was 22±12%. Follow-up was complete in 122 patients (99%).

**Results:** The overall 6-year survival was 31±5% (Figure 1), 56% of deaths being non-cardiac. In multivariate analysis, predictive factors of late mortality were the presence of lower limb arteritis (p=0.04), a lower baseline aortic valve area (p<0.001), higher prevalence of access-complicating P AD (p=0.048), a lower baseline aortic valve area (p<0.001), higher post-T AVI systolic pulmonary artery pressure (p=0.015) and post-T AVI paraprosthetic aortic re-occlusion >1/4 (p=0.015). Event-free survival rate according to Valve Academic Research Consortium-2 (VARG-2) criteria was 28±4% at 5 years. Finally, the rate of good functional results, defined as survival in NYHA class I or II, was 32±5% at 5 years. In the survivors the EQ-5D questionnaire further confirmed the benefit in terms of quality of life.

**Conclusion:** Despite a high-risk profile, one third of patients discharged alive after TAVI were still alive at 6 years. The survivors exhibited good functional results assessed by NYHA class and quality of life standardized evaluation.

**P1408 | BEDSIDE**

**Impact of previous acute pulmonary oedema after transcatheter aortic valve implantation: insights from FRANCE 2 Registry**

A. Furuta, G. Mulliet, J. Dubois-Rande, E. Teiger, Mondor Biomedical Research Institute, Cardiology, Creteil, France

**Objectives:** The aim of this study was to assess the influence of previous clinical history of acute pulmonary oedema (PO) in severe aortic stenosis (AS) patients undergoing transcatheter aortic valve implantation (TAVI).

**Background:** The prognostic value of previous PO has not been thoroughly investigated in a large cohort of TAVI-patients.

**Methods:** Data were analyzed for 3195 patients enrolled in the French national TAVI registry, FRANCE2. We compared the clinical outcome of enrolled patients divided broadly into three groups according to the frequency of previous acute PO episode: group 1: no episode, group 2: single episode, group 3: multiple episodes within the year preceding TAVI.

**Results:** Of the 3195 patients (mean age: 82±7.2 years, mean logistic EuroSCORE: 21.8±14.3 with TAVI, 1880 (58.8%) had no episode, 937 (29.3%) single episode, and 378 (11.9%) multiple episode. Both 30-day and cumulative 1-year mortality increased significantly across the 3 groups (7.7% vs. 9.2% vs. 15.9%; p<0.001, 14.0% vs. 19.4% vs. 24.1%; p<0.001, respectively). In addition, single-PO was not independently associated with an increased mortality at 30-day and 1-year compared to no-PO (HR: 1.01; 95%CI: 0.77-1.33; p=0.935, HR: 1.17; 95%CI: 0.96-1.42; p=0.123, respectively). In contrast multiple-PO was independently associated with an increased risk of both 30-day and cumulative 1-year mortality (HR: 1.60; 95%CI: 1.17-2.1; p=0.004, HR: 1.35; 95%CI: 1.05-1.73; p=0.019, respectively).

**Conclusion:** In conclusion, a history of previous multiple-PO within the year preceding TAVI, but not single-PO, is independently associated with increased mortality at short- and mid-term follow up. Taking previous PO history into consideration might play a crucial role in the selection process in this real-world clinical practice and might contribute as one of the major independent predictors allowing a useful risk-stratification tool for TAVI selection patients and outcome. Then, TAVI should be considered early in patients with AS, when possible, in those with no or single PO episode.
Frailty is a determinant of survival in elderly patients with symptomatic severe aortic stenosis: a prospective study

P1412 | BEDSIDE


Background: The improvement of left ventricular ejection fraction (LVEF) in patients with impaired left ventricular function and severe aortic stenosis (AS) after transcatheter aortic valve replacement (TAVR) is highly variable. There is currently no baseline variable that reliably predicts the improvement of LVEF in patients with TAVR. Methods: Two-year follow-up prospective study of 438 patients over 75 years of age who underwent TAVR and were followed until death or last visit in 2017. The LVEF was assessed before and at 12 and 24 months after TAVR using echocardiographic measurements. Results: Two-year follow-up of 261 patients showed that 46% of patients had an increase in LVEF of 15% or more, 29% showed a decrease, and 25% showed no change. The baseline LVEF was significantly higher in patients with an increase of LVEF than in those with a decrease or no change. Conclusion: The improvement of LVEF after TAVR is highly variable and depends on several baseline variables, such as the severity of AS and the presence of comorbidities.

Frailty is an independent mortality-related factor. Frailty should be considered as a treatment-stratifying factor in older patients with symptomatic severe aortic stenosis.

P1412 | BEDSIDE


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Frailty is an independent mortality-related factor. Frailty should be considered as a treatment-stratifying factor in older patients with symptomatic severe aortic stenosis.
with diagnostic or interventional catheters that may impede straightforward intervention. This has to be taken into account prior to TAVI implantation, especially in the treatment of younger patients suffering from coronary artery disease.

P1414 | BEDSIDE
Pregnancy in the congenital long-QT syndrome: efficacy and safety of beta-blocker therapy for prevention of lethal ventricular arrhythmias
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Purpose: Pregnancy is known as a considerable risk of lethal cardiac events having ventricular tachycardia and syncpe in patients with congenital long-QT syndrome (LQTS). Although β-blocker (BB) is the most effective and commonly used agents to prevent lethal ventricular arrhythmias in LQTS, the efficacy and safety of BB therapy during pregnancy in LQTS is still unclear. In this study, we investigated the effect of β-blocker pregnancy intervention on QT interval and arrhythmia risk of LQTS patients, and the efficacy and safety of BB for pregnancy in the LQTS patients and their infants.

Methods: A retrospective analysis was performed on patients with congenital LQTS who had ever been pregnant, and total 72 pregnancies in 34 LQTS patients (28±4 years old) including 23 genotype-determined (8 LQT1, 13 LQT2, 1 LQT1+3, 1 LQT7) and 11 genotype-unknown were enrolled. We evaluated clinical and electrophysiological characteristics of patients and their pregnancy outcome in presence (BB(+); n=16) or absence of BB therapy (BB(-); n=56).

Results: Nineteen (26%) LQTS patients had taken a BB therapy but 3 of them (11%) discontinued BB for pregnancy despite having ever experienced syncpe and ventricular tachycardia. Follow-up ECG during pregnancy was able to be evaluated in 17 LQTS patients including 8 BB(+) and 9 BB(-). No significant differences were observed in the QT interval before pregnancy (baseline) between the two groups. Six months after pregnancy, the QT interval was not altered in both groups, whereas heart rate was decreased in BB(+) group (71±6 to 64±6 bpm; p=0.01) but not in BB(-) group (67±10 to 72±9 bpm; p=0.3). Thus, the QT interval was significantly shorter in BB(+) compared to BB(-) group (467±35 ms vs. 520±50 ms; p<0.05). Although the history of cardiac events before pregnancy was extremely higher in BB(+group compared to BB(-) group (100% vs. 43%, p<0.001). Three (9%) patients, all in BB(+) group, had lethal cardiac events during pregnancy but none in BB(-) had any cardiac events. Spontaneous abortion occurred in 8 pregnancies but its frequency was not different between two groups. In the perinatal clinical findings, the birth weight was smaller and the gestational week was shorter in BB(+) group than in BB(-) group. No significant differences in maternal complications were observed in the fetal distress and congenital malformation between two groups.

Conclusions: BB therapy during pregnancy may be tolerated for fetus as well as decrease the risk of cardiac events in the LQTS patients suggesting that higher BB therapy patients had better continue BB therapy even for their pregnancy.
Efficacy of quinidine in Brugada syndrome and frequent ventricular arrhythmias episodes

Methods: In conscious goats without electrical remodeling (NR, n=11) and after 3 days or less in postoperative AF. Like in other antiarrhythmic compounds, its effect on CV, AFCL or RP was found. Unsuccessful cardioversion of persistent AF was not related to loss of antiarrhythmic effect on CV, AFCL or RP.

Results: In SR dogs, only the higher dose of GS-458967 (0.1 mg/kg/5') reduced by 86s) at the higher dose. After 10 days of AF, cardioversions occurred in 5 out of 9 animals. The arrhythmic score (AS) was calculated as the average of the most severe outcome within 10': being no ectopic beat (no EB: 1 point) single (sEB: 2 points) or multiple EBs (mEB: 3-5 points). Beats of TdP (8-50 ms) and number of TdPs (50-100 points) were counted. Results: In SR dogs, only the higher dose of GS-458967 (0.1 mg/kg/5') reduced (p<0.05 vs SR) the arrhythmia parameters: QTc, LV MAP and RV MAP (from 297±10, 199±13, 180±8 ms, respectively), at a similar plasma concentration (4.5±0.5 nm). GS-458967 (0.1 mg/kg/5') totally abolished TdP (4/6 after dovetilide vs. 0/6), and reduced AS (1.3±0.4 vs baseline, 3.1±3.3 after dofetilide and 1.9±1.0 after GS-458967; p<0.05 vs baseline and GS-458967). Only some sEB remained present. In addition, in the presence of dofetilide, GS-458967 did not significantly reduce repolarization parameters, such as QTc interval (620±40 ms after dofetilide vs. 594±35 ms after GS-458967).

Conclusions: This study demonstrates that selective blockade of the late sodium current 1) shortens the repolarization duration in SR dogs, and 2) is very effective in terminating dovetilide-induced TdP in CAVB dogs.

Efficacy of vernakalant during 250ms cycle length pacing and AF at different stages of remodeling

Results: A total of 23 patients were identified, mean age 41±13 years, 19 (82%) were male. The ICD had been implanted for secondary prevention in 13 patients (57%), siocone with VA inducible during electrophysiology study in 7 (30%) and for primary prevention in 3 (13%). Quinidine administration was started due to arrhythmia storm in 6 (26%) patients, frequent ICD shocks in 17 (74%). Median time from ICD implant to quinidine administration was 21.5 months (IQR 14.5-50.5). Quinidine bisulfate was prescribed in 8 patients at a mean dose of 570±247 mg/day, and hydroquinidine in 15 patients at a mean dose of 715±338 mg/day. After a mean follow-up of 17±4 months under quinidine we observed a significant reduction in the mean number of shocks from 5 shocks per patient (IQR 3.5-7) to a median of 0 (IQR 0-0). A total of 6 patients experienced VA (5 patients with persistent AF, 10 days, 10) the effects on CV, AFCL and cardioversion efficacy were studied. Also the rate-dependency of the electrophysiological effects was investigated.

Results: Vernakalant caused a dose-dependent effect on RP, CV and AFCL at all stages of remodeling. Its effects on CV, RP and AFCL were preserved after ER (table) and after 10 days of AF. No rate dependent effect of vernakalant on ER (CV) was observed. The median duration of AF paroxysms in ER goats were significantly reduced from 277s (IQR: 25-462s) at baseline to 34s (IQR: 21-86s) at the higher dose. After 10 days of AF, cardioversions occurred in 5 out of 9 animals. The arrhythmic score (AS) was calculated as the average of the most severe outcome within 10': being no ectopic beat (no EB: 1 point) single (sEB: 2 points) or multiple EBs (mEB: 3-5 points). Beats of TdP (8-50 ms) and number of TdPs (50-100 points) were counted. Results: In SR dogs, only the higher dose of GS-458967 (0.1 mg/kg/5') reduced (p<0.05 vs SR) the arrhythmia parameters: QTc, LV MAP and RV MAP (from 297±10, 199±13, 180±8 ms, respectively), at a similar plasma concentration (4.5±0.5 nm). GS-458967 (0.1 mg/kg/5') totally abolished TdP (4/6 after dovetilide vs. 0/6), and reduced AS (1.3±0.4 vs baseline, 3.1±3.3 after dofetilide and 1.9±1.0 after GS-458967; p<0.05 vs baseline and GS-458967). Only some sEB remained present. In addition, in the presence of dofetilide, GS-458967 did not significantly reduce repolarization parameters, such as QTc interval (620±40 ms after dofetilide vs. 594±35 ms after GS-458967).

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ment as significantly regulated pathways. ACADS, ADIPQ, COL6A1, COMP, MAPK9, MYBPC3, PDI A3 and TFBI were among the 28 targets that were equally affected at transcriptome and proteome level.

Conclusion: Dronedarone therapy, although lacking significant effects on infarct size 28d post infarct, provokes significant changes in myocardial gene expression. These changes might improve LV performance in the long term.

P1424 | BENCH 
Dose-dependent inhibition of IKur vernakalant does not elicit an atrial positive inotropic effect
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Purpose: The multi ion channel blocker Vernakalant has recently become available in Europe. Among others, Vernakalant inhibits IKur, which would lead to delayed early repolarization and potentially restore atrial contractility. The purpose of this study is to assess the positive inotropic effect of Vernakalant.

Methods: In 10 goats, the atria were instrumented with piezoelectric crystals, unipolar electrodes and a right atrial pressure catheter. In awake goats, the atrial effective refractory period (AERP) and hemodynamic parameters such as developed pressure (∆P), fractional shortening (FS) and atrial work index (AWI) were assessed for the right atrium at baseline and at 2 and 4 clinically relevant dosages of Vernakalant. Experiments were performed in control (CTL) condition and after 24 hours of AF (24hAF). Subsequently, after 5 half-lives AF was re-induced for 24 hours and monophasic action potentials were recorded in an open chest study under anesthesia.

Results: At baseline, high dose Vernakalant increased the AERP from 136.±19ms to 167.±269ms (p<0.001). After 24hAF AERP decreased to 53.±15ms. High dose Vernakalant caused an increase in AERP comparable to CTL, to 103.±28ms (p<0.01). Hemodynamically, Vernakalant significantly increased atrial segment lengths by 4-8%, therefore leading to a small degree of stretch. However, Vernakalant did not affect ∆P in CTL and 24hAF. Furthermore, no differences in FS and AWI in sinus rhythm or during 450ms cycle length pacing were observed in CTL or in 24hAF atria. Importantly, early repolarization was not affected, indicated by the unchanged degree of repolarization within the first 50ms of the action potential (70±20, 67±12 and 56±15% for baseline, low and high dose, respectively).

Conclusion: Vernakalant increases atrial stretch and prolongs AERP. However, Vernakalant does not have an atrial positive inotropic effect due to the effect on early repolarization.

P1425 | BENCH 
Effects of cilostazol on a canine right ventricular wedge model of Brugada syndrome
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Purpose: To date there is no recommendation of oral drugs that can be used for effective prevention of ventricular fibrillation (VF) in patients with Brugada syndrome (BS). Cilostazol, an oral phosphodiesterase type III inhibitor, is reported in cases to prevent VF in patients with BS, however, the underlying mechanism is poorly understood. We used arterially-perfused RV wedge preparations to investigate the electrophysiological effect of Cilostazol in a BS model.

Methods: BS model was created on 16 arterially-perfused canine right ventricular wedge preparations. Pinacidil at Smmol/L, Terfenadine at Smmol/L and Pilsicainide at Smmol/L were simultaneously perfused. Once BS model stabilized, the 16 preparations were divided into 2 groups: in one group, perfusion was continued with the aforementioned drugs (Control group); in another group, Cilostazol at 10μmol/L was added (Cilostazol group). Transmembrane action potential was recorded from epicardium and endocardium of the wedge preparation, as well as pseudo-ECG. Program stimulation was performed. Spontaneous or induced arrhythmia events were registered.

Results: In arterially-perfused canine RV wedge BS model, Cilostazol corrected J point elevation, decreased transmural and epicardial regional dispersion of repolarization, and was associated with less arrhythmia events (Table 1).

Conclusion: Cilostazol may prevent VF in BS by offsetting the electrophysiological abnormalities, especially the widened transmural dispersion of repolarization.

P1426 | BENCH 
Mechanoelectrical feedback alterations induced by the benzothiazepine derivative JTV-519
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1 University of Valencia, Department of Physiology, INCLIVA, Valencia, 2 University of Valencia, Department of Physiotherapy, Valencia, 3 Polytechnic University of Valencia, Electronic, Valencia, 4 University of Valencia, Department of Physiology, Valencia, 5 University Hospital Clinic of Valencia, INCLIVA, Valencia, Spain

Purpose: To analyze the effects of mechanical stretch on myocardial activation during ventricular fibrillation (VF) in an isolated and perfused rabbit heart model in order to compare the responses obtained under the influence of a drug (JTV-519) that act on the intracellular Ca2+ dynamics and to determine whether the electrophysiological effects of stretch are modified by this benzothiazepine derivative that inhibits ryanodine receptor opening probability and sarcoplasmic endoplasmic reticulum Ca2+ ATPase pump activity.

Methods: In twenty six Langendorff-perfused rabbit hearts VF recordings were obtained using epicardial needle electrodes on the left ventricle free wall under coronary perfusion during arrhythmia. After the induction of VF, stretching was applied and maintained for ten minutes and after this period, local stretching was removed. VF dominant frequency (spectral techniques) was determined each minute during the study protocol.

Results: JTV-519 slowed the arrhythmia during baseline recordings (control dominant frequency = 14±3±3 Hz vs JTV-519 1 microM dominant frequency = 6.6±0.9 Hz, p<0.001, and JTV-519 0.1 microM 10.8±0.9 Hz, p<0.05). The VF acceleration observed in the control series during stretch was abolished in the 1 microM JTV-519 series and diminished in the 0.1 microM JTV-519 series (41% increment in the control series, 2% increment in the 1 microM JTV-519 series, p<0.0001 vs control and 20% increment in the 0.1 microM JTV-519 series). After suppressing stretch in the control series dominant frequency returned to values similar to baseline (post-stretch = 13.7±2.6 Hz, ns vs baseline), while in the 1 microM JTV-519 series there was a significant dominant frequency decrease in the post-stretch state (post-stretch = 5.9±0.8 Hz, p<0.05 vs baseline). No decrease was found in the 0.1 microM JTV-519 series (post-stretch= 10.2±1.0 Hz, ns vs baseline).

Conclusion: The benzothiazepine derivative JTV-519 modifies the baseline VF activation patterns slowing the arrhythmias and at the highest studied concentrations abolishes the cardiac electrophysiological modifications produced by acute myocardial stretching.

P1427 | BENCH 
Therapeutic doses of ranolazine prolong ventricular action potential duration with a frequency-dependent effect without modifying calcium transient duration
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1 Polytechnic University of Valencia, ITACA, Valencia, 2 University of Valencia, Physiotherapy, Valencia, 3 Research Foundation Hospital of Valencia (INCLIVA), Physiopathology, Valencia, 4 University of Valencia, Physiology, Valencia, 5 Research Foundation Hospital of Valencia (INCLIVA), Medicine, Valencia, Spain

Purpose: Ranolazine is an antianginal drug that has been shown to effectively protect against atrial and ventricular arrhythmias in clinical and experimental studies. However, the mechanisms by which ranolazine exerts its arrhythmia effects are not completely understood. Our aim was to analyze the effects of ranolazine administration at therapeutic doses on action potential and calcium transient duration in ventricular myoccardium.

Methods: We analyzed 20 Langendorff-perfused rabbit hearts using simultaneous voltage and calcium optical mapping during control conditions (n=11) and 5μM ranolazine (RNZ, n=9) continuous perfusion. The electromechanical uncoupler blebbistatin, the voltage dye di-4-ANBDPO and the calcium dye Rhod-2 AM were used. External stimuli (2 ms duration, twice the diastolic threshold) were applied in the output tract of the right ventricle by means of a bipolar electrode at a frequency of 4, 5, 6, 7 and 8 Hz. Optical movies were recorded using a 128x128 pixel EMCCD camera at 1 kHz sampling frequency. The optical transient duration at 80% of repolarization (APD80) for the voltage signal and the [Ca2+]i transient duration at 80% return to baseline (CaT80) were computed. Data were reported as mean±SD. A mixed model ANOVA with repeated measures in one

<table>
<thead>
<tr>
<th>No. of preparations</th>
<th>Control Group</th>
<th>Cilostazol Group</th>
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<tr>
<td>QT (ms)</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>JT (ms)</td>
<td>228±12</td>
<td>274±18</td>
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<td>J point elevation (ms)</td>
<td>0.48±0.12</td>
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<td>Transmural dispersion of repolarization (ms)</td>
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<td>Epicardial regional dispersion of repolarization (ms)</td>
<td>76±18</td>
<td>32±16</td>
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<td>Endocardial regional dispersion of repolarization (ms)</td>
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<td>VT/VF incidence (episode)</td>
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<td>Endocardial ERP (ms)</td>
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<td>Epicardial ERP (ms)</td>
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<tr>
<td>Dispersion of ERP (ms)</td>
<td>5±10</td>
<td>5±10</td>
</tr>
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</table>

TP<0.05. ERP, effective refractory period.
factor (frequency) was used to assess differences between groups with a two-tailed alpha level of P < 0.05.

**Results:** Epicardial optical APD80 was not different between control and RNZ groups when the longest pacing cycle lengths (4 and 5 Hz) were used. However, when hearts were challenged with pacing at shorter cycle lengths, APD80 significantly increased in the RNZ group at 6, 7 and 8 Hz (109.3±3 vs 104.6±6 ms at 6 Hz, 104.4±6 vs 95.5±5 ms at 7 Hz and 94.5±4 vs 88.8±4 ms at 8 Hz; P < 0.05 vs control). With respect to calcium dynamics, values of CaT80 were not different between control and RNZ groups at all the pacing frequencies studied.

**Conclusions:** In our experimental model, ranolazine administered in a therapeutic dose (31μM) prolongs action potential duration in ventricular myocardium at high pacing frequencies, without modifying calcium transient duration. This increase in action potential duration could be involved in the antiarrhythmic effects of ranolazine.

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**P1429 | BEDSIDE**

**Correlation between colchicine effects on early atrial fibrillation recurrence after ablation and left atrium epicardial adipose tissue volume**

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**Background:** The epicardial adipose tissue (EAT) has been shown to release activated pro-inflammatory cytokines and EAT was associated with the development of atrial fibrillation (AF). Immediate recurrence of AF after AF ablation was related with inflammatory process. Colchicine after AF ablation could suppress the inflammatory reactions and AF recurrence. We evaluated the correlation between colchicine effects on AF recurrence within 2 weeks following AF ablation and various inflammatory factors, including EAT volume surrounding left atrium (LA-EAT volume).

**Methods:** We studied 35 patients who received colchicine treatment with 0.5 mg/day for 2 weeks from the next day after AF ablation. The study patients underwent 256-row multi-detector computed tomography before ablation. LA-EAT was automatically identified using the threshold attenuation values of -50 to -200 Hounsfield unit. LA-EAT volume was measured by semi-automatically tracing axial images from the bifurcation of the pulmonary artery to the coronary sinus. We compared LA-EAT volume, hs-CRP (pre-ablation, 2 days and 2 weeks after ablation) and body temperature during hospital between AF recurrence group (AF >30 sec) and non-AF recurrence group within 2 weeks after AF ablation.

**Results:** LA-EAT volume was significantly lower in non-AF recurrence group (n=29) than in AF recurrence group while the other factors were similar. (Table).

**Conclusion:** Colchicine treatment after AF ablation may suppress the incidence of early AF recurrence in the patients with lower LA-EAT volume.

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**P1431 | BEDSIDE**

A neuroendocrine basis for the underlying mechanisms of dysautonomic syndromes in syncope: the SYSTEMA cohort

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**Purpose:** Syncope (sudden transient loss of consciousness due to cerebral hypoperfusion) with rapid recovery affects ~4% of the population but mechanisms remain elusive. This study aimed to evaluate haemodynamics and cardio-vasoactive biomarkers during passive orthostasis preceding syncope.

**Methods:** 687 consecutive patients (298M, 369F; 55-159 years) were recruited. Blood samples were taken simultaneously during head-up tilt test (HUT). Blood samples during supine rest before HUT and after 3 min of 70° tilt were used for determination of plasma epinephrine, norepinephrine, renin, C-terminal-pro-arginine-vasopressin (CT-proAVP), C-terminal-endothelin-1 (CT-proET-1), and mid-regional-fragment of pro-atrial-natriuretic-peptide (MR-pro ANP) in both positions. Beat-to-beat blood pressure (BP) and ECG were continuously recorded for 20 min or until spontaneous syncope (Italian Protocol) yielding baseline+3 min tilt haemodynamics, systolic (SBP), diastolic (DBP) and heart rate (HR), plus maximal deviations from baseline during tilting. Multivariate age-sex-adjusted linear regression assessed associations between baseline biomarkers, haemodynamics and HUT changes.

**Results:** Higher resting CT-proET-1 predicted decrease in SBP (1SD: -3.72, SE=0.97mmHg; p<0.001) and DBP (β-coefficient = -2.14, SE=0.48mmHg; p<0.00001) during HUT. Decrease in SBP and DBP at 3 min HUT paralleled increased CT-proAVP (1SD: β-coefficient = -2.43, SE=0.69mmHg; p<0.001, and β-coefficient = -1.69, SE=0.33mmHg; p<0.0001, respectively). Lower resting MR-proANP predicted increase in HR at 3 min HUT (1SD: β-coefficient = -1.28, SE=0.41ppm; p=0.002), maximal increase in HR during HUT paralleled increased norepinephrine (1SD: β-coefficient = 1.79, SE=0.47ppm; p<0.01).

**Conclusions:** Elevated rest endothelin-1 occurs in orthostatic hypotension, while progressive upright vasopressin shows possible compensation against hypotension preceding syncope, while progressive upright HR increase is paralleled by norepinephrine release, possibly compensating inadequate vasoconstriction and tachycardia.
Conclusions: 1. The brain saturation changes induced by syncope during HUTT are related to the age of patients with vasovagal faints. 2. The youngest and the oldest patients are more sensitive to brain hyperperfusion related to the vasovagal syncope. 3. Lower degree of desaturation induced by syncope in the middle aged patients might reflect the ability to autoregulate brain perfusion or other mechanism, i.e. kind of preconditioning.

PI434 | BEDSIDE
Features and pregnancy outcomes in women with the syndrome of postural orthostatic tachycardia
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Background: Postural orthostatic tachycardia syndrome (POTS) is characterized by the increase in heart rate over 30 beats per minute when standing up. Postural orthostatic tachycardia syndrome is much more common in women than in men. Pregnancy exacerbates POTS, however, there is not enough observation and evidence on the course and outcome of pregnancy for women with POTS.

Aim: Study the characteristics and pregnancy outcomes in women with POTS.

Methods: POTS was traced during pregnancy in 25 women (25.5±2.3 years), who also had POTS before. During pregnancy, these women were observed in the cardiac center every three months. Women were also observed after a year delivery (after 3, 6, 9 and 12 months).

ECG monitoring, blood pressure monitoring, evolution of autonomic function at supine rest and 5 minute passive tilt (Taskforce, CNSsystem, Austria) were made.

Results: POTS increased in 20 patients (80%) during pregnancy. Hypotension before syncope was reported in 18 women. Pregnancy-related hypotension was reported in 20 women. 12 women had reflex syncope before pregnancy, 3 of them had syncope during pregnancy. Syncope first appeared in 3 women. Increased values of spontaneous baroreflex were observed in pregnancy with significant reduction of baroreflex sensitivity during tilt. All women were recommended to wear compression elastic stockings. Compression elastic stockings were worn by 15 women (80%). They have seen an increase in diastolic and systolic blood pressure during the daytime (p<0.01). These women also decreased the clinical symptoms of orthostatic failure.

Beta-blockers have been assigned to 10 women. Five women were wearing compression knitted fabrics as well as using beta blockers. Five women refused to decrease the clinical symptoms of orthostatic failure.

Conclusion: Pregnancy exacerbates POTS, however, there is not enough observation and evidence on the course and outcome of pregnancy for women with POTS.

Conclusion: Pregnancy exacerbates POTS, however, there is not enough observation and evidence on the course and outcome of pregnancy for women with POTS.

P1435 | BEDSIDE
Management of syncope: Remote telemetry counseling patients with syncope in the emergency department of our region based on the guidelines of the European Society of Cardiology

Aim: Diagnosis of syncope based on ESC recommendations in remote telemetry consultation patients in Emergency Departments (EDs) of our region.

Methods: Regional Cardiological Center performs remote telemetry consultation in 27 EDs in our region with population of 1.7 million people. Patients (pts) with syncope delivered in EDs between March, 1st, and April, 1st, 2012 were all included in a prospective observational study. Consulting physicians have learnt diagnostic standards of ESC. EDs reported primary diagnosis (ECGs, blood pressure, and standard electrocardiogram) to the remote telemetry office. Consultants made recommendations about pts examination and treatment if the primary examination did not reveal cause of syncope. Patients with syncope of unknown cause were hospitalized in a specialized cardiological center if necessary.

Results: 935 patient consultations were held in the remote center from our region ED during the month, there of 135 pts had syncope (14.4%, median age 73, interquartile range 18-85, 62% women). 37.0% of patients had arrhythmogenic syncope. 40.4% of patients had neurocardiogenic reaction. 22.3% pts had bradyarrhythmias, 12.5% tachyarrhythmia and 2.2% pacemaker failure. 3.2% of pts had drug-induced syncope. Cardiovascular diseases were the cause of syncope in 15.5%. Reflex syncope was observed in 18.5% and orthostatic hypotension in 10.4% of pts. Autonomic failure due to chronic alcohol intoxication was present in 3.0% of pts. 6.8% of pts were "non-syncope". Unexplained syncope was found in 8.8% of pts.

Conclusion: Remote telemetry consultations allow diagnosis of syncope in hospitals located in rural areas in accordance with the recommendations of ESC. Arrhythmogenic syncope prevailed in connection with the specific references in EDs.

P1435 | BEDSIDE
Tilt testing results are related to the tilt table properties
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The tilt testing environment and equipment used can influence the characteristics of syncope. Various tilt tables have different lowering times. There are no unequivocal data regarding the results of tilt testing performed under such different conditions. In particular there are no clear observations of self-perpetuating asystole in the setting of persisting tilt.

The aim of the study was to compare the results of tilt testing performed on two different tilt tables. The study group consisted of 824 patients (618 F and 206 M), aged 41.4±14.2 years, diagnosed because of syncope. Patients were divided in two groups according to the tilt table: group I (644 pts) had the tilt testing performed with the table with 47 seconds lowering time and group II (180 pts) was tested with tilt table with 10 seconds lowering time.

The multivariate regression revealed that the duration of loss of consciousness (dLOC) was positively related only to VASIS type of neurocardiogenic reaction and to the type of tilt table.

Conclusions: Longer lowering time during tilt testing increases the percentage of vasovagal type of neurocardiogenic reaction. Various tilt tables have different lowering time influencing duration of loss of consciousness during syncope. Duration of RR pause during cardioinhibitory type of syncope remains unaffected by lowering time indicating its independent mechanism.
Remote vs. conventional follow-up of implantable loop recorders: time to diagnosis and overall diagnostic yield is similar

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Purpose: Implantable loop recorders (ILR) are endorsed by ESC guidelines for the investigation of syncope. Remote monitoring of ILRs may improve diagnostic yield. We investigated time to diagnosis and diagnostic yield of remote monitoring compared to conventional follow-up.

Methods: Patients receiving Medtronic Reveal XT ILR were prospectively enrolled to remote monitoring (Medtronic Carelink Network). Scheduled transmissions were made weekly for 8 weeks and monthly thereafter. Patients were asked to monitor additional transmissions following symptoms. Comparison was made retrospectively to the previous 100 consecutive patients followed non-remotely.

Results: 25 patients were enrolled to remote monitoring, 60% were female, median age was 48.7 years with mean follow-up of 443.2±140.6 days. The conventional follow-up cohort consisted of 100 patients, 62.7% were female, median age was 54.0 years, mean follow-up 393.4±248.2 days.

In the remote group 18 of 25 patients (72%) had ≥1 symptomatic episode; a diagnosis was made in 12 patients (48%). In the control group, 61 patients had ≥1 symptomatic event resulting in a diagnosis in 37 (37%) patients (p=0.314). The types of diagnoses in the remote follow-up group were sinus node disease (SND) in 1 patient, AF in 2 patients, vasovagal syncope (VVS) in 2 patients, complete heart block (CHB) in 1 patient; 6 patients had typical symptoms without any significant arrhythmia. In the control group, 3 patients had SND, 4 AF, 6 VVS, 2 CHB, and 2 SVT; the remaining 19 patients had typical symptoms without any arrhythmia.

Mean time to diagnosis was 257.6±188.7 days in the remote arm vs. 171.6±147.7 days in the control group (p=0.03). Time to first symptom was similar in both groups. The difference in mean time of ILR data transmission between the remote group (5.7±8.1 days vs. 23.9±17.1 days s, p<0.001) the majority of the delay in the remote group was delay in patient transmission of data.

Compliance with remote monitoring was excellent and patient satisfaction was rated highly.

Conclusions: Remote monitoring of ILRs allows rapid assessment of symptomatic events but diagnostic yield and time to diagnosis is similar to non-remote follow-up. This may be related to the greater contribution of symptomatic episodes (rather than automatically detected episodes) to diagnosis in both groups.

Evaluating brain desaturation during head-up tilt test in teenagers with suspected vasovagal syncope


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Brain hypoperfusion, causing the syncope, may lead to changes in the brain tissue. The question is how differ teenagers response to the brain hypoperfusion in relation to older group of patients with syncope.

Aim of study: Analysis of changes of cerebral regional oxygen saturation (rSO2) measured by near-infra-red spectroscopy (NIRS) during head-up tilt test (HUTT) in young patients with vasovagal syncope (VVS).

Study population: We observed 507 pts.: 151 young pts. (107 girls) aged 12-18 yrs (Group I) and 356 adult patients (248 women) – Group II - with VVS referred to HUTT.

Methods: All pts underwent HUTT according standard Westminster protocol. During HUTT rSO2 of frontal lobes of brain was measured using INVOS cerebral desaturation analyzer (Cotechini, Italy).

Results: HUTT was positive in 131 pts. from group I (86,8%) and 285 pts. from group II (80,1%). Significant desaturation preceded syncope induction during HUTT in all pts in comparison to pts with negative test (-29,6 and -31,8% vs -11,4 and -12,1% p<0.00001). Higher values of mean desaturation and area limited by maximal rSO2 were observed in teenagers in comparison to adult pts. with vasovagal syncope induced by HUTT. (rSO2-mean L 7,8% vs 5,7%; rSO2-mean R 7,7% vs 5,4%, p<0.02; rSO2-AUC 187,7 vs 153,3±min; 204,8 vs 149,5±min, p<0.015). There were no significant differences of maximal desaturation between both groups.

Conclusions: Syncope induced by Head-Up Tilt Test lead to more pronounced cerebral desaturation in teenagers than in adult people. 2 Higher brain desaturation caused by hypoperfusion leading to reflex syncope in young patients might be a potential injuriant factor for the nervous tissue in this group of patients.

Age-dependent differences in tilt-testing results and RAAS activation in patients with vasovagal syncope

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The inappropriate activation of the renin-angiotensin-aldosterone system (RAAS) could lead to haemodynamic disturbances resulting in a syncope. The aim of the study was to assess the activation of RAAS during the tilt-induced syncope with regard to the type of a neurocardiogenic reaction and the age of studied patients.

The study population consisted of 641 patients (211 M, 430 F) aged 43.7±18.4 years, with the syncope during diagnostic tilt testing. Aldosterone concentration (ALDO) was measured in a supine position before the test (ALDO 1), immediately after the syncope (ALDO 2) and 10 minutes after the syncope (ALDO 3). Patients were divided into 4 groups according to quartiles of age. Results are shown in the table. There were no differences between the age quartiles with regard to tilt testing results according to VASIS classification. The older groups of patients showed less pronounced RAAS activation irrespective from VASIS classification.

Table 1

<table>
<thead>
<tr>
<th>Age quartile/VASIS (%)</th>
<th>ALDO 1 (pg/ml)</th>
<th>ALDO 2 (pg/ml)</th>
<th>ALDO 3 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>261.3±198.1</td>
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<td>64.3±34.4*</td>
<td>126.1±72.5*</td>
<td>167.8±83.9*</td>
</tr>
<tr>
<td>100.8*</td>
<td>66.6±47.7*</td>
<td>157.1±100.0*</td>
<td>183±100.8*</td>
</tr>
</tbody>
</table>

Conclusions: RAAS activation during tilt-testing-induced syncope decreases with older age. This phenomenon do not influence the type of neurocardiogenic reaction. The implementation of therapeutic measures based on water and salt supply could be more effective in older patients with vasovagal syncope.

Remote vs. conventional follow-up of implantable loop recorders; time to diagnosis and overall diagnostic yield is similar

P1438 | BEDSIDE

Thoracic impedance to characterize hemodynamic changes preceding syncope

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Purpose: Shifting of thoracic blood volume from the thorax to the lower extremity is a well known mechanism of neurally mediated syncope (NMS), a condition often resulting in falls and accidents. We previously demonstrated the feasibility of accurate prediction of NMS based on heart rate and pulse wave characteristics. The aim of the present study was to examine whether thoracic impedance (THI), a surrogate parameter of thoracic fluid content is suitable for assessment of hemodynamic changes preceding syncope.

Methods: In 44 patients with a history of unexplained syncope diagnostic 70° head-up tilt table testing (HUTT) was conducted, following current ESC guidelines. Heart rate, beat-to-beat plethysmographic blood pressure and THI were continuously recorded. THI as a 30 s average during HUTT was compared among baseline (tilt up -1 min), early tilt (tilt up +1 min) and late tilt (tilt back -1 min). ROC analysis was employed to determine predictive power in respect to occurrence of syncope.

Results: In 21 (48%) patients (57±18 years, 8 females) HUTT was positive, resulting in induction of syncope. In 15 of these patients (71%) syncope occurred following nitrate challenge. Mean time to syncope onset was 43.9±4.9 min after tilting. In both groups a conclusive rise in THI during tilting could be observed (p<0.0001), with no significant difference between groups (p=0.7991).

Using the absolute difference of THI over time proved to be a robust measure of THI changes, with the development during HUTT (THI early vs. late) being the most accurate predictor of syncope occurrence. Choosing a cut-off value of 1.7424 a sensitivity of 76.2% and a specificity of 55.0% could be achieved.

Conclusion: Thoracic impedance is useful to characterize hemodynamic changes preceding syncope during tilt table testing. As THI can be easily and reliably measured and is less prone to artifacts than measurement of pulse wave characteristics, it might improve acute syncope prediction. Further studies, integrating both methods might result in more robust algorithms and thus could foster the reliable application of this technology in ambulatory patients.

Utilization of implantable loop recorders in children with long QT syndrome

P1441 | BEDSIDE

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Purpose: Prior research has demonstrated high efficiency of the implantable loop recorder (ILR) in identifying causes of syncope and palpitation in children and adults. Long-term ECG monitoring using ILR was proposed for studying a cause of syncope in children with LQTS.

Materials and methods: ILRs were implanted in 12 children with LQTS from 11 unrelated families. Mean age at implantation was 10±4 years (from 2.5 to 16), 58% were boys. Four pts had experienced syncope and all pts were treated with beta-blockers. There were no indication for ICD implantation before-

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term ECG monitoring was initiated. The ILR follow-up period was 24±8 months on average (from 4 to 35 months).

Results: After IRL implantation 5 of 12 pts experienced syncope (3) or pre-syncope (2) episodes. Two patients showed episodes of sustained self-terminated ventricular fibrillation (VF) during syncope. The duration of VF was up to 67 ms. Both were implanted with ICD. The third patient was diagnosed with reflex asystole. He had two subsequent episodes of asystole lasted 52 and 168 ms provoked by venipuncture. As he had LQT3, the ICD was implanted. Two patients had demonstrated recurrent episodes of pre-syncope that coincided with palpitations and tachycardia with heart rate of about 35 bpm.

Conclusion: In children with LQT3, implantable loop recorders can provide valuable information for identification of the cause of syncope. It permits to distinguish arrhythmic and vasovagal mechanisms what is important for choosing adequate strategy of treatment.

P1442 | BEDSIDE Reduced Baroreflex sensitivity during head-up tilt test in patients with vasovagal syncope

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Purpose: The evidence is conflicting regarding the role of baroreflex in patients with vasovagal syncope. The aim of the study was to measure baroreflex sensitivity (BRS) and other hemodynamic parameters during head up tilt test (HUT) with nitroglycerine stimulation.

Methods: Nineteen asymptomatic patients. HUT was performed in 51 patients with the history of recurrent syncope (mean age 46±19 years, 18 men, 23 women). Cardiac output (CO), stroke volume (SV), left ventricular ejection time (LVEF) and total peripheral resistance (TPR) were assessed during HUT by volume-clamp method using a beat- to beat photoplethysmography. Spontaneous baroreflex sensitivity was computed using a sequential BRS calculation.

Results: HUT was positive in 28 patients and negative in 23 patients. Baroreflex sensitivity (expressed as proportion of baseline value) was significantly lower at the time of syncope in HUT positive group when compared to end test values in HUT negative group (0.54±0.27 vs. 0.72±0.35, p<0.03). CO was significantly lower in HUT positive patients compared to HUT negative patients (2.6±1.4 vs. 4.3±1.4 l/min, p<0.001), similarly as SV (34.7±14 vs. 49.2±19 ml, p<0.005), LVEF and significantly higher in syncope patients (2.82±2.6 vs. 240.5±58.8 ms, p<0.002) and TPR did not differ between two groups of patients at the time of syncope.

Conclusion: Reduced baroreflex sensitivity may contribute to the development of the vasovagal syncope by inability to adequately counteract hypotension resulting from decreased cardiac output at the time of syncope.

P1436 | BENCH Myeloperoxidase-deficiency protects from ventricular tachycardia in a murine model of ischemic cardiomyopathy

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Background: Leukocytes have emerged as important mediators of adverse myocardial remodeling following myocardial infarction. Myeloperoxidase (MPO), a heme enzyme abundantly expressed and released by polymorphonuclear neutrophils (PMN), exerts pro-inflammatory and pro-fibrotic properties and has been identified to be causally linked to the formation and propagation of various cardiovascular disorders. We disclosed recently, that MPO critically promotes atrial fibrosis and arrhythmias. Thus, we sought to investigate whether MPO might also influence structural and electrical remodelling in ventricular myocardium.

Methods and results: Wild-type C57Bl6/J (WT) and MPO-deficient (Mpo−/−) mice underwent either sham surgery (n=7, 6) or ligation of the left descending coronary artery (LAD) (n=7, 5). Right ventricular electrophysiological investigations 3 weeks after LAD ligation disclosed profoundly increased vulnerability for ventricular tachycardia (VT) in infarcted WT as compared to Mpo−/− mice (number of VT episodes: 6.7±1.3 vs. 1.8±0.9, p<0.01, sham: 2.0±0.4 vs. 1.7±0.8, p<0.79; total time of VT episodes: 3.67±0.88 vs. 0.86±0.36 sec, p<0.05, sham: 0.70±0.18 vs. 1.07±0.75 sec, p=0.67). Epicardial mapping analyses indicated a decreased ventricular velocity and enhanced degree of electrical conduction in WT as compared to Mpo−/− mice. No differences were observed in infarct size between WT and Mpo−/− mice, as assessed by hematoxylin/eosin stain of myocardial sections.

Conclusions: The current data demonstrate, that MPO increases the vulnerability for ventricular arrhythmias in a murine model of ischemic cardiomyopathy. Whereas no differences were observed in infarct size, characteristics of electrical conduction pointed to aggravated adverse electrical or structural remodeling in WT as compared to Mpo−/− mice. While the underlying mechanisms still have to be elucidated, the results underline the important role of inflammatory processes in cardiac remodeling upon myocardial infarction and identify MPO as a potential therapeutic target to prevent ventricular arrhythmias in ischemic cardiomyopathy.

P1444 | BENCH Mosaic reciprocal chain deficiency due to induced mtDNA deletions in the mouse heart leads to an increase in inducible ventricular arrhythmias after myocardial ischemia/reperfusion

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Purpose: In the heart, mitochondrial dysfunction occurs physiologically during aging as shown by a low cytochrome c oxidase activity in single scattered cells in vitro (COX- cells). Recent studies have shown that few COX- cells are suffi- cient to induce spontaneous arrhythmias in aged old animals. Here, we investigated the inducibility of arrhythmias in these younger mice with structural heart disease due to myocardial infarction, which do not exhibit spontaneous arrhythmias.

Methods: A cell-type specific knockin strategy was used to generate a mouse model that expresses a dominant-negative mitochondrial Tom20 heli-

case (K320E mutation; delTwinkle) in the heart (Rosa26-floxed-Stop-delTwinkle x MCK-Cre). At the age of 12 month coronary myocardial infarction was induced in all mice using a 3mm stamp to generate a structural heart disease and myocardial scar. 2 weeks after the operation we performed in vivo electrophysiological investigations using transvenous right heart catheterization to determine surface and intracardiac electrocardiogram (ECG) parameters. Ventricular extrastimulus pacing and burst stimulation maneuvers were used to evaluate ventricular vulner-

Results: At the age of 12 month, delTwinkle mice exhibited 50% increased levels of mtDNA deletions (qPCR; p<0.05) but no generalized mitochondrial de-

fect as indicated by unchanged protein levels and normal activities (spectropho-
tometry) of five oxidative phosphorylation complexes. COX- cardiomyocytes were found in 0.17% (±0.12) in hearts of delTwinkle while such cells were never seen in control hearts. Compared to controls, no alterations in standard surface ECG parameters, atrial and ventricular refractory periods, as well as in sinus-node and AV-node function were observed. However, the probability of induction of ventricu-

lar tachycardias (VTs) was significantly higher in delTwinkle mice compared to controls (10.5% vs. 3.2%; p<0.04). VTs could be induced in 56% of all delTwinkle mice and in only 40% of control mice.

Conclusions: The existence of coexistence of two new emerging COX- cardiomyocytes due to the accumulation of mtDNA deletions is associated with inducible arrhythmias after myocardial infarction without accompanying alterations in electrophysiological parameters. Mitochondrial DNA deletions, as found in the aging
heart, might therefore promote arrhythmias in the elderly population beyond structural heart disease.

**P1447 | BENCH**

Beta-blockers do not prevent the pro-arrhythmic action of high-level sympathetic stimulation: a role for neuropeptide Y?

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**Purpose:** Beta-blockers (BB) are the only anti-arrhythmic drug that improve mortality in patients with ischaemic heart disease, but a significant risk of arrhythmia remains. During high-level sympathetic drive, such as during myocardial infarction, blockade of the β1-receptor (β1-R) can be released by norepinephrine. NPY is a potent vasococontractor that can also reduce parasympathetic activity and alter cardiac electrophysiology. We hypothesised that ventricular fibrillation threshold (VFT) would be reduced following high-level sympathetic stimulation even in the presence of a BB. We also investigated whether NPY is independently pro-arrhythmic and decreases VFT, and if this mechanism is mediated by the Y1 or Y2 receptor.

**Methods:** Hearts with intact stellate ganglia (SG) and sympathetic innervation were isolated from male Sprague Dawley rats (250-300g) and Langendorff perfused in constant flow mode. VFT was determined by pacing at a fixed cycle length (150 ms x 20 beats) followed by a 5sec 50Hz burst at increasing current amplitude (mA) until sustained VF was induced. VF was cardioverted with 1ml of potassium chloride solution (50mmol/L). A control experiment demonstrated that VF was fully blocked over 3 successive inductions (n=6). SG were stimulated at 10Hz, 1ms pulse width (above capture voltage). Drugs were perfused for 15 mins before stimulation. Electrical restitution (RT) was derived from optically mapped action potentials. All data are presented as mean±standard error.

**Results:** Direct SG stimulation significantly increased heart rate and left ventricular developed pressure (LVDP) and these changes were completely blocked by metoprolol (10μmol/L). However, 2 mins of RSG stimulation in the presence of metoprolol still significantly reduced VFT by over 50% (2.49±0.49 to 1.28±0.26mA, n=5). A similar result was observed following 2 mins stimulation of the left SG. Exogenous NPY (250nmol/L, n=6) also significantly reduced VFT by 50% (2.4±0.15 vs 1.2±0.12mA) and increased coronary vascular resistance and LVDP. The action of NPY on VFT, CVR and LVDP were abolished by the Y1 receptor antagonist BIB0203 (1μmol/L, n=6), but not by the Y2 receptor blockade with BIB2024 (1μmol/L, n=6). Preliminary analysis of RT by optical mapping is suggestive of a steepening of the curve with NPY 250nmol/L (0.27±0.04 vs NPY 0.42±0.12, n=4).

**Conclusion:** Pro-arrhythmic sympathetic stimulation remains pro-arrhythmic in the presence of BB, implicating sympathetic co-transmitters as a novel arrhythmic trigger. NPY can directly decrease VFT via a Y1 receptor mediated mechanism and steepens the RT curve.

**P1448 | BENCH**

Acetylcholine-dependent potassium current determines atrial defibrillation threshold by regulating post-shock refibrillation

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**Purpose:** Termination of atrial fibrillation (AF) by electrical cardioversion (ECV) remains the mainstay of AF treatment in symptomatic patients. Still, standard ECV attempts may be below atrial defibrillation threshold (aDFT) and hence unsuccessful in up to 20% of patients. However, increasing ECV energy in such instances causes significant tissue damage. Continuous high frequency activation with KCNJ5 shRNA containing lentiviral vectors confirmed these results. Therefore, we investigated the effects of IK,ACh blockade on aDFT in AF.

**Methods:** Neonatal rat atrial cardiomycocyte monolayers were burst paced to induced frequency-based AF and subjected to biphasic truncated exponential shocks (10-ms duration, t1=20-100V (10V increments) to determine aDFT. To study the effects of IK,ACh on the CT, cultures were treated with Tertiparin or transient transduction with lentiviral vectors encoding KCNJ5-specific shRNAs. Optical mapping was used to assess electrophysiological parameters prior to, during and after ECV attempts.

**Results:** Successful ECV depended on complete synchronization of all phases around ECV attempts. Successful ECV decreased aDFT (32±11 vs 60±25 in controls). Transduction with KCNJ5 shRNA containing lentiviral vectors confirmed these results.

**Conclusions:** These results suggest that remodeling of IK,ACh could increase aDFT by shortening of wavelength during reentry and thereby decrease ECV succeessrate. Hence, this study provides new mechanistic insight into failing ECV and identifies IK,ACh as a possible atrium-specific target to increase efficacy of ECV while decreasing its harmfulness.

**P1449 | BEDSIDE**

Arrhythmias occurrence relations with angiotensin 2 levels in hypertensive patients

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**Activity of renin-angiotensin-aldosteron system play significant role in development of cardio-vascular diseases and particularly in development of hypertensin. Arrhythmias development in hypertensive patients also determined by renin-angiotensin system activity.**

The purpose of our study was to evaluate the role of angiotensin 2 (AT2) activity in development of electrophysiological remodelling in hypertensive patients.

**Methods:** We examined 196 patients with arterial hypertension 1-3 grade complicated by HF-I-II NYHA functional class. The mean age of patients - 52.2 (6.8) years. Patients with acute myocardial infarction in history, diabetes mellitus and autoimmune diseases were excluded from the study. In all patients was performed 12 standard leads, Holter ECG monitoring, EchoCG (ASE/EAE recommendations 2005) and were evaluated plasma levels of AT2 (ng/l). AT2 levels equal to 10-30 ng/l were defined as low and AT2 levels > 30 ng/l were defined as high. HF NYHA functional class was determined by using the 6MWTS. Extrasystoles types were determined by Lown B. classification. Mean ejection fraction - 65.8 (5.7%).

The comparison of frequency of arrhythmias occurrence in hypertensive patients with different levels of AT2 was performed by χ2 test. Statistical significance was defined at the level of methods for p<0.05.

**Results:** As it can be seen from table 1, the frequency of occurrence of frequent supraventricular premature beats, frequent ventricular extrasystoles and ventricular extrasystoles 3-4 grade was statistical significant higher in patients with high levels of AT2.

<table>
<thead>
<tr>
<th>AT2 levels &amp; arrhythmias occurrence</th>
<th>P</th>
<th>Angiotensin 2 levels x2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All SVPB</td>
<td>62 (67%)</td>
<td>77 (74%)</td>
<td>0.76 0.38</td>
</tr>
<tr>
<td>Rare SVPB</td>
<td>44 (48%)</td>
<td>43 (49%)</td>
<td>0.05 0.81</td>
</tr>
<tr>
<td>Frequent SVPB</td>
<td>18 (19%)</td>
<td>34 (31%)</td>
<td>4.3 0.03</td>
</tr>
<tr>
<td>All atrial extrasystoles</td>
<td>52 (56%)</td>
<td>67 (64%)</td>
<td>1.65 0.19</td>
</tr>
<tr>
<td>Rare atrial extrasystoles</td>
<td>37 (40%)</td>
<td>38 (36%)</td>
<td>0.28 0.59</td>
</tr>
<tr>
<td>Frequent ventricular extrasystoles</td>
<td>15 (16%)</td>
<td>29 (28%)</td>
<td>3.97 0.05</td>
</tr>
<tr>
<td>Ventricular extrasystoles 3-4 grade</td>
<td>12 (14%)</td>
<td>25 (22%)</td>
<td>3.86 0.04</td>
</tr>
</tbody>
</table>

SVPB, supraventricular premature beat.

**Conclusion:** Thus, our study indicates role of high levels (>30 ng/l) of AT2 in arrhythmias development in hypertensive patients.

**P1450 | BENCH**

Remodeling of calcium handling proteins during atrial fibrillation complicated by tachymyopathy in a porcine model

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**Background:** Atrial fibrillation (AF) and heart failure (HF) are two of the most frequent cardiovascular diseases. They often coexist and lead to significant morbidity and mortality. Recent evidence suggests a key role for Ca2+ handling abnormalities in the perpetuation and progression of AF. Despite the clinical significance of this dual epidemic, AF-associated remodeling of atrial Ca2+ cycling in the presence of HF has not been addressed to date.

**Methods:** Persistent AF was induced in domestic pigs by atrial burst pacing via an implanted cardiac pacemaker. Animals underwent electrophysiological and echocardiographic examination on day 1 and prior to euthanization (day 7). Expression of Ca2+ handling proteins was analyzed in right atrial tissue samples obtained from pigs with persistent AF (day 7; n=5) and compared to untreated control pigs in sinus rhythm (SR; n=5).

**Results:** During AF animals displayed significantly reduced left ventricular ejection fraction (LV-EFDay 1: 73±6%; LV-EFDay 7: 58±8%) and prolonged atrial fibrillation refractory periods. Persistent AF and HF were associated with down-regulation of Ca2+-dependent protein kinase II (CaMKII) by 37% without affecting the auto-phosphorylation state of CalMII at Thr286. We further observed suppression of PKAII (-62%), L-type calcium channel (L TCC) subunit δ (Ca2+L TCC δ) by 25% with the auto-phosphorylation state of Ca2+-calmodulin-dependent kinase II (CaMKII) by 25%. Expression of NCCx was increased by 400% compared to controls. In contrast, expression of Serca2a, phosphorylated ryanodine receptor at Ser2814 and L TCC δ was not significantly altered.

**Conclusions:** In conclusion, AF produces distinct remodeling of Ca2+ handling...
proteins in the presence of tachycardia that is different from paroxysmal or persistent AF in the absence of relevant structural heart disease. These findings highlight the complexity of electrical remodeling processes and provide a starting point for more personalized understanding of AF pathophysiology and treatment efficacy in HF patients.

**P1451 | BENCH**

Low proarrhythmic potential of escitalopram and citalopram in contrast to the proarrhythmic potential of zopiclone: study on significant QT-prolongation

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**Background:** In several case reports proarrhythmic effects of citalopram and escitalopram were reported. The aim of the present study was to investigate if application of citalopram, escitalopram or haloperidol have the potential to provoke polymorphic ventricular tachycardia in a sensitive model of proarrhythmia.

**Methods and results:** In 20 female rabbits, citalopram or escitalopram (2 μM and 4 μM, n=10) were infused after baseline data. Eight endo- and epicardial monophasic action potentials and a simultaneously recorded 12-lead ECG showed a significant QT prolongation after application of citalopram as compared with baseline (2 μM: +7 ms, 4 μM: +66 ms, p = 0.05) accompanied by an increase of action potential duration (APD90: +18 ms, 2 μM citalopram; +27 ms with 4 μM citalopram). Administration of haloperidol also increased dispersion of repolarization (2 μM: +12 ms, 4 μM: +12 ms, p = ns). Lowering of potassium concentration in bradycardic AV-blocked hearts provoked early afterdepolarizations (EAD) in 3 of 10 hearts and polymorphic ventricular tachycardia resembling tordes de pointes in only 1 of 10 hearts (4 μM, 22 episodes). Application of escitalopram also increased QT-interval (2 μM: +8 ms, 4 μM: +30 ms, p = 0.05) and APD90 (2 μM: +5 ms, 4 μM: +2 ms, p = 0.05) without significant effects on dispersion of repolarization (2 μM: +5 ms, 4 μM: +7 ms, p = ns). No proarrhythmia was observed in this group. The results were compared to 10 rabbits treated with haloperidol (1 μM and 2 μM). Haloperidol led to an increase in QT-interval (1 μM: +51 ms, 2 μM: +85 ms, p = 0.05) and APD90 (1 μM: +30 ms, 2 μM: +36 ms, p = 0.05). In addition, haloperidol increased dispersion of repolarization (1 μM: +7 ms, 2 μM: +40 ms, p = 0.05) and led to the occurrence of EAD in 7 of 10 and of polymorphic ventricular tachycardia in 5 of 10 hearts (69 episodes) with 2 μM haloperidol after lowering of potassium concentration.

**Conclusion:** In the present study, application of citalopram only caused polymorphic ventricular tachycardia in 1 of 8 hearts while escitalopram did not induce proarrhythmia despite significant QT prolongation. In contrast, haloperidol led to a more marked prolongation of myocardial repolarization combined with a marked increase of dispersion of repolarization. These results imply that application of citalopram or escitalopram is not as proarrhythmic as some case reports might suggest while haloperidol is torsadogenic.

**P1452 | BENCH**

Herg blockade by iboga alkaloids

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**Purpose:** The iboga alkaloids are a class of naturally occurring and synthetic compounds, some of which modify opiate withdrawal or self-administration of abused substances in humans and/or animal models. Fatalities, and case reports describing QT prolongation and PVTs including TdP call attention to the safety of ibogaine, the prototypic iboga alkaloid. We evaluated Herg blockade by ibogaine with purities of 94% and 99.5% derived respectively by extraction from Tabernanthe iboga and by semisynthesis via voacangine: as well as ibogaine’s principal metabolite noribogaine; 18-methoxyconoradine (18-MC), a product of rational metabolism decreases with increasing concentrations .

**Results:** We found that 94% and 99.5% ibogaine block the hERG channel with respective EC50s of 3.53±0.16 μmol/l (n=11) and 4.09±0.69 μmol/l (n=14). Substantial, noribogaine and haloperidol block the hERG channel with respective EC50s of 2.86±0.68 μmol/l (n=11) and 2.25±0.34 μmol/l (n=6). hERG blockade was similar among the 4 drugs (one-way ANOVA, p = 0.05). 18-MC to the limit of solubility decreased hERG with an estimated EC50 between 50 μmol/l and 100 μmol/l (n=6).

**Conclusion:** 18-MC is possibly a safer congener and a candidate for development. The EC50s of ibogaine and noribogaine appear clinically relevant regarding levels associated with QT prolongation, PVTs, and/or fatalities observed in patients. Noribogaine, with a 1/2 in humans on the order of days may mediate delayed fatalities following the ingestion of ibogaine.

**P1453 | BENCH**

Disparate effect of single dose and co-administration of clarithromycin and furosemide on cardiac gene expression (Kcnq1, Cacna1c, Myh6, Myh7 and Myh7b) in beta-adrenergically stimulated hearts

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**Purpose:** In presence of hypokalaemia, the use of QT-prolonging clarithromycin can lead to Torsades de Pointes (TdP). Sustained prolongation of repolarisation may affect cardiac performance that is usually under control of calcium regulation proteins as well as myosin heavy chains (MHCs). We tested levels of mRNA expression of K channel genes, intracellular Ca2+ regulating genes and also MHCs genes in beta-adrenergically stimulated as well as in non-stimulated hearts.

**Methods:** Wistar rats were treated for 7 days with clarithromycin (CLA, 200 mg/kg/d, p.o.), furosemide (FUR, 200 mg/kg/d, p.o.) or both (CLA+FUR). Controls (CON) received vehicle. ECG was monitored under basal conditions and under cumulative isoproterenol stimulation (IS) doses of 5-60 ng/min (i.v.) in anaesthetised animals. Using qRT-PCR we examined the left ventricular expression of the following genes: Kcnh2 (RERG1), Kcnq1 (KVLQT1), Cacna1c (LTCC α1C subunit), Atp2a2 (SERCA2a), Ryr2 (ryanodine receptor 2), Myh6 (alpha-MHC), Myh7 and Myh7b (beta-MHCs).

**Results:** As expected, furosemide caused hypokalaemia (P < 0.05). Both, clarithromycin as well as furosemide decreased hERG channel activity with respective blocking effect of 18-MC.

**P1454 | BENCH**

Genetic aspects of arrhythmias

**P1455 | BEDSIDE**

Ethnicity and phenotype in the SCNSA E1784K mutation

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**Purpose:** Long QT (LQTS) and Brugada syndromes (BrS) are arrhythmia syn-
dromes with highly variable penetrance. The E1748K mutation in SCN5A is the most commonly identified mutation in both LQTs and BrS and causes an over-lap syndrome. Carriers within the same pedigree may exhibit LQTs phenotype, BrS phenotype or both. This international project characterized a unique cohort of E1748K carriers in order to identify associations between phenotype and eth-nicity.

**Methods:** 133 E1748K mutation carriers belonging to 38 families from 5 different countries including Japan were included. Data was collected on age, gender, symptoms, family history and the ECG. Non-digital and digital ECG data were analysed using proprietary software. At least 2 readings were taken per variable and the mean value used. BrS was defined as a type 1 ECG pattern that was spontaneous or induced by a class 1 antiarrhythmic. Statistical significance was determined using either the 2-tailed t-test or Chi-squared test as appropriate.

**Results:** Among the 133 E1748K mutation carriers, spontaneous BrS and longer QTc intervals were more evident in the Japanese carriers who were more symptomatic albeit without prior aborted SCD. Drug-induced BrS phenotype was un-masked in 63% of Caucasians (34/54) who underwent a test. However, a family history of other SCD was present in 50% of Caucasian families compared to only 13.6% of Japanese families (p=0.015). Results are summarised in Table 1.

**Conclusions:** There is significant variation in expression of E1748K between ethnicities with varying severity and prior symptomatology. This supports a strong role for genetic modifiers of phenotype and risk which deserves further study.

**Table 1**

<table>
<thead>
<tr>
<th>Age (years, mean, range)</th>
<th>29, 1-70</th>
<th>30, 1-70</th>
<th>30, 1-70</th>
<th>427, 150-70</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex-male (%)</td>
<td>66, 50</td>
<td>50, 48</td>
<td>50, 48</td>
<td>50, 48</td>
</tr>
<tr>
<td>Spontaneous BrS (%)</td>
<td>8, 6</td>
<td>1, 1</td>
<td>7, 2</td>
<td>0.0001</td>
</tr>
<tr>
<td>PR (ms, mean, range)</td>
<td>170, 128-302</td>
<td>171, 104-302</td>
<td>165, 128-191</td>
<td>0.5098</td>
</tr>
<tr>
<td>QRS (ms, range)</td>
<td>94, 60-136</td>
<td>89, 60-120</td>
<td>95, 64-136</td>
<td>0.0002</td>
</tr>
<tr>
<td>Pre-syncope/syncope (%)</td>
<td>23, 11, 17</td>
<td>17, 11, 12</td>
<td>11, 12, 40</td>
<td>0.0271</td>
</tr>
<tr>
<td>Aborted SCD (%)</td>
<td>4, 3</td>
<td>4, 3</td>
<td>0, 0</td>
<td>0.2731</td>
</tr>
</tbody>
</table>

**P1456 | BENCH**

Allelic variations in hERG expression discriminates between symptomatic and asymptomatic LQT2 patient-hiPSC derived cardiomyocytes

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**Purpose:** PRKAG2 mutation is responsible for a rare autosomal dominant cardiac glycogenosis. Clinical manifestations associate ventricular pre-excitation (VPE) syndromes with hypertrophic cardiomyopathies (HCM). The evolution can be complicated with Brugada-like (AV) blocks, severe heart failure episodes and sudden deaths (SCD). We aimed to describe the natural history of this disease in 9 French families.

**Methods:** A cohort of 34 patients from 9 families was diagnosed between 2001 and 2010 in the laboratory for molecular diagnosis of HCM at Pitié-Salpêtrière Hospital. Whereas 5 families carried the recurrent p.Arg302Gln mutation, 4 families private mutations including 3 unreported. A survival study with Kaplan-Meier curves and LogRank tests allowed the calculation of the hazard ratios associated with the clinical hallmarks of the PRKAG2 syndrome at 40 years of age. We also compared clinical characteristics of p.Arg302Gln patients (21 patients, 62% of the cohort), vs newly identified mutations patients (13 patients).

**Results:** Hazard ratios for a 40 year old patient: VPE 70% (99%-CI: 50%-87%), HCM 66% (99%-CI: 8%-61%), AV blocks 22% (99%-CI: 9%-46%), SCD 20% (99%-CI: 8%-42%), device implantation (pacemaker or defibrillator) 25% (99%-CI: 2%-48%). Heart transplant was realised in 2 patients at 55 and 60 years of age. The median age at death was 60 years. Ablation procedures of the VPE were complicated with AV blocks in 4/18 patients, requiring a cardiac device implantation. Between patients carrying the recurrent mutation and private mutations, no significant difference was identified regarding the development of VPE, the presence of a HCM, severe heart failure, complications or death. A trend toward a lower risk of HCM was identified in p.Arg302Gln mutation patients compared to other mutations.

**Conclusion:** This is the first study to describe the clinical evolution of the PRKAG2 syndrome in a large cohort of 35 carriers issued from 9 families. Complications may occur spontaneously but AV blocks can be favoured by VPE ablation attempts. Prognosis is severe with a natural history of the disease in favour of a high risk of death in this cohort.

**P1458 | BEDSIDE**

Andersen-Tawil syndrome - symptomatology and prognosis in seven affected families

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**Purpose:** Andersen-Tawil Syndrome (ATS) is a rare genetic disease caused by a mutation in KCNJ2. It is characterized by arrhythmias, U-waves in ECG, periodic paralysis and developmental abnormalities. Diagnosis and treatment can be difficult due to varied symptomatology and unknown prognosis. Unnecessary ablations and ICD implantations are not rare. The aim of the study was to evaluate ATS symptomatology and prognosis in 7 affected families.

**Methods:** 7 probands with pathogenic mutations in KCNJ2 and 23 first degree relatives were examined. Clinical and ECG analysis, genetic screening, pedigree analysis and Holter studies in symptomatic carriers were performed. Group 1 included 17 mutation carriers (age 27.3±14.7, 29.4% males). Group 2 consisted of 13 unaffected relatives (age 28.8±21.6, 38.5% males).

**Results:** Gr.1 prevalence of dysmorphic features was: clinodactyly of fingers – 91.7% (CI: 81%-100%), syndactyly of toes –11.8%, primary dentoalveolar in the 3rd decade of life –11.8%, low-set ears –5.9%. Clinodactyly was observed in one non-carrier (7.7%). The height and weight of adults were 158.3±6.5cm, 52.4±7.7kg in Gr.1 and 70.4±8.9cm, 74.4±18.9kg in Gr.2, (p<0.001 and <0.001, respectively). Neurological manifest-
tations (41.2%) and syncope (24.9%) were observed in patients with mutations. ECG results are presented in Table. Each of 8 Holter studies revealed BVT, VES (200–3300/24h) and VT (120–170/min) in 7 pts. SCD was reported in 3 non-genotyped relatives: two of them in the family with the coexisting LQT2 mutation. The triad of manifestations appeared only in probands. In one family, pedigree analysis revealed a de novo mutation.

Conclusions: In our ATS cohort: 1) The most prevalent dysmorphic manifestations were clindacyclotonia and micrognathia; 2) The presence of giant U-wave, prolonged QTU interval, but not long QT interval, was typically observed, though it appears also in relatives without the mutations; 3) ATS could be caused by a de novo mutation; 4) SCD was rare. Decisions about ICD implantation and ablation must be done cautiously.

P1459 | BEDSIDE Cardiac sodium channel gene mutations associated with dilated cardiomyopathy

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Background: Mutations in the cardiac sodium channel gene, SCN5A, cause a variety of inherited arrhythmic syndromes. However, the relationship between the SCN5A gene mutations and left ventricular (LV) dysfunction is still unclear.

Methods and results: We screened the SCN5A gene in 693 probands associated with phenotypes that indicated sodium channel loss-of-function mutations such as Brugada syndrome (BrS), cardiac conduction disease (CCD), sick sinus syndrome (SSS), idiopathic ventricular fibrillation (IVF) and atrial fibrillation (AF).

In this cohort, we identified SCN5A mutations in 41 probands (21 in BrS, 14 in SSS, 4 in AF, 14 in CCD, and 3 in IVF, including overlap syndrome). Four of 41 patients were associated with decreased LV systolic function (R1023C in 2 patients, D127SN and W1345F in one patient, respectively). One of the R1023C mutation carrier was 46 yo male diagnosed with arrhythmogenic right ventricular cardiomyopathy with LV involvement, and the other R1023C carrier was 75 yo female associated with complete atrio-ventricular block and severe LV dysfunction. The patient with a D127SN mutation was 61 yo female suffered from AF and SSS, and her LV function was decreased. The W1345F carrier was 71 yo male. He received a pacemaker implantation due to SS and his LV EF was decreased to 30%.

Conclusions: In this study, approximately 10% (4/41) of the patients with SCN5A mutations who presented with sodium channel loss-of-function phenotypes were associated with LV dysfunction. Further experiments will be needed to reveal the underlying mechanisms of SCN5A-related cardiomyopathy.

P1460 | BENCH Aging-related atrial and ventricular transcriptomic changes in the rat heart. Implications for cardiac arrhythmias


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Purpose: Aging is associated with significantly increased prevalence of cardiac arrhythmias, but transcriptional events that underlie this process remain to be established.

To gain insight into molecular mechanisms of aging-related cardiac arrhythmias, we performed mRNA expression analysis comparing atrial and ventricular myocardiun from healthy Wistar-Kyoto (WKY) rats of different ages.

Methods: Atrial and ventricular sampling was performed in 3 groups (n=4 each) of young (14-week-old), adult (25-week-old), and aging (47-week-old) WKY rats. mRNA expression of 49 genes involved in cardiac arrhythmogenicity were investigated using TaqMan Low Density Array analysis.

Results: Of the 89 studied genes, 40 and 64 genes presented steady atrial and ventricular expressions, respectively. All genes differentially expressed within the atria of WKY rats were up-regulated with advancing age, mainly the genes encoding for Na+ currents, Ca2+, Na+ channels, and type 1 collagen. Atrial expression levels of 16 genes were positively correlated with age. Ventricular transcriptomic analysis revealed a balance between up-regulated and down-regulated genes encoding for the same ion channels. Aging atria displayed a transcriptomic profile consistent with higher propensity to arrhythmias, including up-regulation of genes encoding for If, Ica-L, Ica-T, Na+ outward K+ currents, and collagen, while ventricular transcriptome did not seem to be significantly altered by aging.

Conclusions: Our results indicate the induction of an up-regulation transcriptional response in atrial but not ventricular myocytes with advancing age, suggesting that the two chambers undergo different molecular remodeling process. Additionally, the present results could partly explain the higher propensity to atrial than ventricular arrhythmias in the elderly.

P1461 | BENCH CaMKII inhibition prevents ventricular and supraventricular tachyarrhythmias in a murine model of recessive CPVT


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Purpose: Bidirectional ventricular tachycardias (VT) are considered a main finding in patients with catecholaminergic polymorphic VT (CPVT). However, CPVT exposes patients to sudden cardiac death. Adrenergically mediated atrial tachycardias (AT) are also common manifestations of the disease. It has been suggested that the sarcoplasmic reticulum Ca2+ leak induced by β-adrenergic stimulation is mediated preferentially by Ca2+- dependent sarcoplasmic reticulum Ca2+ leak induced by adrenergic signaling. Therefore we aimed to investigate the role of CaMKII in atrial arrhythmias.

Methods: A novel SCN4B intronic variant identified in patients with Brugada syndrome and idiopathic ventricular fibrillation caused an exon 3 deletion. In our ATS cohort: 1) The most prevalent dysmorphic manifestation was atrial tachycardia; 2) The triad of manifestations appeared only in probands. In one family, pedigree analysis revealed a de novo mutation.

Conclusions: Our results indicate the induction of an up-regulation transcriptional response in atrial but not ventricular myocytes with advancing age, suggesting that the two chambers undergo different molecular remodeling process. Additionally, the present results could partly explain the higher propensity to atrial than ventricular arrhythmias in the elderly.
from control samples and performed RT-PCR. To confirm the splice error, we constructed a minigene system including the variant, and it was transfected into human embryonic kidney (HEK293) cells and analyzed.

Results: We identified one SCN4B intronic variant in 6 patients (5 BrS and 1 IVF, 2% of cohort) and summarized the clinical data in Table. The variant was not seen in 240 controls and is located in intron 3, c. 463 + 3 a–t. We could Obtain cDNA of SCN4B from cardiomyocytes, but not from leukocytes or fibroblasts, indicating the tissue specific expression of the gene. Minigene system confirmed that the variant caused an exon 3 skipping. This would cause a deletion of 229 nucleotides and thereby a premature stop codon with frame shift (c. 225_463del, p. Leu155Trpfs*8).

Clinical characteristics of carriers

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Sex</th>
<th>Symptom</th>
<th>ICD Diagnosis</th>
<th>Heart rate (beats/min)</th>
<th>PR (ms)</th>
<th>ORS (ms)</th>
<th>QT (ms)</th>
<th>QTc (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37/M</td>
<td>Syncope</td>
<td>BR</td>
<td>160</td>
<td>100</td>
<td>400</td>
<td>380</td>
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</tr>
<tr>
<td>2</td>
<td>60/M</td>
<td>Syncope</td>
<td>BR</td>
<td>50</td>
<td>200</td>
<td>100</td>
<td>420</td>
<td>380</td>
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<tr>
<td>3</td>
<td>32/M</td>
<td>Asympt.</td>
<td>BR</td>
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<td>CPA</td>
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<td>5</td>
<td>44/M</td>
<td>CPA</td>
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<td>74</td>
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<td>100</td>
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</table>

M, male; CPA, cardio-pulmonary arrest; NA, not available.

Conclusion: We identified an SCN4B intronic variant, c. 463 + 3 a–t, which would result in a skipping of exon 3, thereby leading to the premature termination of Nav1.4, and its decreased expression would be related to BrS or IVF occurrence. No SCN4B mRNA is expressed in leukocytes or fibroblasts.

P1465 | BENCH
Novel abnormally splicing variants identified in induced pluripotent stem cells derived iPSC cardiomyocytes from a long-QT syndrome patient with KCNQ1-A344A

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Background: Long-QT (LQT) syndrome is an inherited arrhythmic disorder characterized by prolongation of cardiac action potentials, and an increased risk for life-threatening ventricular arrhythmias. LQT type 1 is the most common type of LQT syndrome, which is caused by mutations in the alpha-subunit of the slow component of the delayed rectifier potassium channel (IKr) gene, KCNQ1. A synonymous mutation (c.1032G>T, p.A344A) in KCNQ1 is located in the 3’end of exon 7, and reported to cause abnormal splicing. We previously reported the abnormal splicing patterns and functional characterization of KCNQ1-A344A using patient’s blood lymphocytes and a heterologous mutant expression system in cultured cells.

Objectives: We aimed to recapitulate the LQT1 phenotype and investigate the disease causing mechanisms of KCNQ1-A344A carriers using human induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs).

Methods and results: We generated iPSCs from peripheral blood lymphocytes obtained from an 11-year-old male carrying KCNQ1-A344A. He experienced syncope while swimming at his teens. Patient 4 consulted a doctor for palpitation and a chest pain. His ECG showed QT prolongation (QTc 480 ms) and his Holter ECG revealed frequent PVCs in Holter ECG in addition to frequent PVCs. Patient 1 admitted an emergency hospital after vomiting and QT prolongation (QTc 510 ms) during exercise. In addition to our previous findings using the blood lymphocyte’s RNA, we identified novel abnormal splicing variants using patient-derived iPSC-CMs (exon 6-7 skipping, exon 6-8 skipping, and insertion of the 5’ end of intron 7). Multi-electrode array (MEA) analyses revealed that isoproterenol caused early afterdepolarization-like waveforms and induced atrial, ventricular and atrioventricular re-entrant tachycardia. Isoproterenol also induced atrioventricular block and atrial fibrillation in the iPSC-CMs. The non-canonical splice variant c.1032G>T, p.A344A is located in C-terminal domain, where many previous mutations were identified. Patient 1 experienced syncope during exercise and was referred to our hospital. He experienced atrioventricular block and atrial fibrillation during exercise. We could obtain cDNA of KCNQ1 from iPSC-CMs and sample from control. We constructed a minigene system including the variant, and it was transfected into human embryonic kidney (HEK293) cells and analyzed. To confirm the splice error, we obtained cDNA of KCNQ1 from cardiomyocytes, but not from leukocytes or fibroblasts, indicating the tissue specific expression of the gene. We newly identified the additional exon skipping and intron insertion in LQT1-iPSC-CMs (40%, n=10 vs. control; 0%, n=8). We identified 15 additional KCNQ1 mutations, and performed RT-PCR. To confirm the splice error, we constructed a minigene system including the variant, and it was transfected into human embryonic kidney (HEK293) cells and analyzed. We could obtain cDNA of KCNQ1 from cardiomyocytes, but not from leukocytes or fibroblasts, indicating the tissue specific expression of the gene. We newly identified the additional exon skipping and intron insertion in LQT1-iPSC-CMs (40%, n=10 vs. control; 0%, n=8).

P1466 | BEDSIDE
Identification of latent mutations in primary inherited arrhythmia syndromes using benchtop next generation sequencer

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Purpose: The genetic analysis has been applicable for the diagnosis and the treatment in primary inherited arrhythmia syndromes. Recently, benchtop next generation sequencers (NGS) have been available for target gene screening. This study aimed to search for the latent mutations in patients with inherited arrhythmias.

Methods: This study consisted of 152 patients diagnosed with inherited arrhythmias (table). They were negative for mutations in target genes of their disease, those were screened by DHPLC, HRM or direct sequencing methods. We designed amplion primers for 47 genes which were reported as causative or suspected genes for primary inherited arrhythmia syndromes. Using TruSeq custom amplicon kit and a BNGS MiSeq system, we performed analyses for our targeted genes. Detected mutations were confirmed by direct sequence methods.

Results: We identified 86 mutations in 70 patients (table). In 62 LQTS patients, we identified 8 RYR2 mutations, which were the major cause of CPVT. Two KCNQ1 mutations identified in LQTS patients were supposed to be overlooked by conventional screening methods. In 19 BrS patients, we identified 3 desmosomal mutations, which would indicate that BrS and ARVC were overlapping. In 10 CPVT patients, we identified 3 RYR2 mutations though no mutation was identified in minor CPVT genes.

Conclusions: We unveiled latent mutations by BNGS in short time. Especially in LQTS, we elucidated the high frequency of RYR2 mutations. However, we need to distinguish the variants identified in this method are truly disease causing or not.
Conclusions: We identified 2 ANK2 mutations in 4 symptomatic patients with inherited tachyarrhythmia using BNGS. Although the genetic screening of ANK2 has been difficult due to the size of the gene, BNGS enables us to screen the gene in short time. Because the number of reported ANK2 mutations in inherited arrhythmias is small, we need to accumulate the patients with ANK2 mutations and explore the mechanism of ankyrin syndrome.

P1467 | BEDSIDE
Identification of novel SCN10A variants in Brugada syndrome patients
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Background: Voltage-gated sodium channels are indispensable for action-potential propagation in human heart. The expression of Nav1.8 in cardiomyocytes has been known, and a polymorphism of SCN10A which encodes Nav1.8 was reported to affect the atrioventricular conduction. In addition, a variant in SCN10A was reported to be associated with Brugada syndrome (BrS). This study aimed to investigate the frequency of SCN10A mutations in Japanese patients with BrS, and among them, the phenotypic differences between patients with other BrS-causative genes.

Methods: The subject of this study consists of 240 Japanese probands suspected as BrS. We screened SCN10A genes using high resolution melting (HRM) analysis. To achieve the reliable detection of rare variants, we analyzed the whole exonic regions of SCN10A in the healthy controls, we checked SCN10A in 250 healthy Japanese subjects. In addition, the possible impact of amino acid substitutions on the structure and function of human protein was evaluated using 3 prediction software packages. Proband we identified 7 CACNA1C mutation carriers and 17 SCN5A mutation carriers in our BrS probands. After gene-screening, we compared the clinical characteristics among probands with gene mutations in SCN10A, CACNA1C or SCN5A.

Results: We identified 5 SCN10A variants in 6 probands (2.5%). Five probands were male. Four probands complained of symptoms; 1 deceased by sudden cardiac arrest at age of 35, 1 suffered ventricular fibrillation (VF) and 2 had recurrent syncope. An electrophysiological study induced reproducible VF in 1 symptomatic proband. Two probands were implanted implantable cardioverter de-fibrillators. Regarding their electrocardiograms, we compared the clinical characteristics among probands with gene mutations in SCN10A, CACNA1C or SCN5A.

Conclusions: We identified 5 novel SCN10A variants in 6 BrS probands. Although the functional significance of these SCN10A variants remains unknown, most of the probands showed severe arrhythmic attacks. Therefore, we should treat these mutation carriers as deleterious clinically.

P1468 | BEDSIDE
Cardiac involvement in familial amyloidotic polyneuropathy

Purpose: Familial Amyloidotic Polyneuropathy (FAP) is a genetic disease with multisystemic involvement, including cardiovascular (CV). The purpose of this study was to evaluate a large contemporary cohort of individuals with FAP in relation to the CV involvement: symptoms, signs of autonomic dysfunction and electrocardiographic (ECG) changes.

Method: Observational, retrospective, single-center study of 664 carriers of FAP related mutations.

Results: In our sample, median age was 38 years (IQ 32-48), 56% were female, 99% were Val30Met TTR mutation carriers and 61% were symptomatic (48% in stage 1, 7% in stage 2 and 5% in stage 3, according to Cotinou stage). During a mean time of disease symptoms of 8.5±5.5 years, 24% started treatment with tafamidis, 27% implanted pacemaker (PM), 18% underwent liver transplantation in a mean time of disease symptoms of 8.9±5.5 years, 99% were Val30Met TTR mutation carriers and 61% were symptomatic (48% in stage 1, 7% in stage 2 and 5% in stage 3, according to Cotinou stage). In addition, the possible impact of amino acid substitutions on the structure and function of human protein was evaluated using 3 prediction software packages. Proband we identified 7 CACNA1C mutation carriers and 17 SCN5A mutation carriers in our BrS probands. After gene-screening, we compared the clinical characteristics among probands with gene mutations in SCN10A, CACNA1C or SCN5A.

Results: We identified 5 SCN10A variants in 6 probands (2.5%). Five probands were male. Four probands complained of symptoms; 1 deceased by sudden cardiac arrest at age of 35, 1 suffered ventricular fibrillation (VF) and 2 had recurrent syncope. An electrophysiological study induced reproducible VF in 1 symptomatic proband. Two probands were implanted implantable cardioverter de-fibrillators. Regarding their electrocardiograms, we compared the clinical characteristics among probands with gene mutations in SCN10A, CACNA1C or SCN5A.

Conclusions: We identified 5 novel SCN10A variants in 6 BrS probands. Although the functional significance of these SCN10A variants remains unknown, most of the probands showed severe arrhythmic attacks. Therefore, we should treat these mutation carriers as deleterious clinically.

P1469 | BENCH
Semiconductor next generation sequencing of the main QT interval duration genes in a cohort of long QT and Brugada Syndrome patients
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Purpose: Mutations at the KCNQ1, KCNQ10, CSNSA, and KCNE1/E2 that encode cardiac channels have been associated with inherited arrhythmias and the QT-interval in the general population. We aim to analyze how Next Generation Se- quencing (NGS) technologies would be of special interest to uncover the genetic variation at these genes in large cohorts of patients with Long QT and Brugada Syndrome (LQTS vs. BrS).

Methods: We developed a protocol for the NGS of the five genes through am- plification of all the coding regions in only two tubes followed by semiconductor array sequencing in an Ion Torrent Personal Genome Machine (PGM). A total of 60 patients (index cases) with LQTS (29) or BrS (31) were NGS sequenced for the five genes.

Results: We identified 25 putative mutations (19 in LQTS and 6 in BrS patients) that were confirmed through Sanger sequencing of the corresponding amplicons: 8 in KCNQ1, 10 in KCNH2, and 7 in SCN5A. In addition, five patients (16%) with a clinical phenotype of BrS were carriers of a rare KCNE2 variant (p.T8A). Their clinical profile included spontaneous type I ECG in 3 cases (60%), syncope in 2 cases (40%), and male gender in 4 cases (80%). History of sudden death of first degree relatives younger than 45 years (age range 13 to 41) was documented in 3 cases (60%). No any of those patients experienced malignant arrhythmias or sudden death. Despite this KCNE2 variant has been linked to prolonged QT interval duration in the general population, we did not find it in any patient with a clinical phenotype of LQTS (p<0.01).

Conclusions: Here we show the usefulness of the NGS procedure to uncover the genetic mutations and variants related to arrhythmogenic syndromes in our population. The method allowed for detection of a genetic variant encoding the aux- iliary β subunit KCNE2 (p.T8A) not previously reported as affecting BrS patients. It is well known how this protein interacts with the potassium transient-outward current, which plays a major role for arrhythmogenesis in BrS. Our data encour- age further analysis about the electrophysiological significance of p.T8A KCNE2 variant in BrS patients.

P1470 | BEDSIDE
Prevalence of early repolarisation in paediatric relatives of sudden arrhythmic death syndrome (SADS) victims

Background and aims: Evaluation of the ECG J-point in the inferior and lateral leads (early repolarisation) has been described in survivors of VF arrest and occurs in adult first degree relatives of sudden cardiac death (SCD) probands at a frequency significantly greater than in controls, raising the possibility that this could represent an independent risk factor in the aetiology of SCD. However, data on early repolarisation in the paediatric population are lacking. This study aimed to assess the prevalence of early repolarisation in paediatric first degree relatives of sudden arrhythmic death syndrome victims.

Methods: Paediatric relatives (age <18 years) of SADS probands referred to the Inherited Arrhythmia Clinic at our hospital had their initial screening ECG reviewed for evidence of J-point elevation. J-point elevation was defined as ST-elevation >1 mm from 42±14 years at baseline. ORS-JS ST slurring or a discrete notch in two or more inferior (II, III, aVF) or lateral (I, aVL, V4, V5, V6) leads.

Results: The ECGs of 95 paediatric first degree relatives of SADS victims from 31 families were reviewed by two assessors. J-point elevation was present in 22 cases (23%) of this patient group compared to the reported prevalence of 5-13% in the general paediatric population.

Conclusions: Infero-lateral J-point elevation occurs in a substantial proportion of paediatric first degree relatives of SADS probands with a similar prevalence.
to that described in adults. This suggests that early repolarisation could be an important inherited trait when evaluating relatives of SADS victims. Prospective follow up of this group of children is important to establish the implication of this finding in future risk stratification.

**P1471 | BENCH**

Recapitulation of lamin A/C-related cardiomyopathy using patient-specific induced pluripotent stem cells: a novel splicing mutation in LMNA

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Mutations in lamin A/C gene (LMNA) are the most common cause of familial dilated cardiomyopathy (DCM) with cardiac conduction system disease (CCD). Here we report a 63-year-old male case suffered from DCM and CCD. The proband's mother, sister, and two sons were also affected with DCM and/or CCD. We identified a novel synonymous mutation, c.1131C>T, p.R377R, in exon 6 in LMNA. The results of genetic analysis with his family members were completely consistent with this mutation. We used the web-based splicing site analysis tool (Berkeley Drosophila Genome Project). The prediction indicated that the LMNA-R377R mutation generates the abnormal boundary of splicing donor site adjacent to the mutated base (score for 3' splice site: 0.91). The abnormal splicing would introduce a frameshift and premature termination in the sequence. We generated induced pluripotent stem cells (iPSC) from peripheral lymphocytes and differentiated into cardiomyocytes (CMs). The beating rate of embryoid bodies generated from patient iPSC was significantly lower than that from control iPSC (Fig. 1). Expression levels of LMNA in patient iPSC-CMs were reduced by half (Fig. 2), which was compatible with the result of peripheral blood lymphocytes.

These findings indicated that the LMNA-R377R synonymous mutation led the cryptic splicing followed by nonsense-mediated mRNA decay in iPSC-CMs from the patient. The iPSC-CMs derived from the patient with lamin A/C-related cardiomyopathy could recapitulate the disease specific phenotype, and are useful to investigate the disease causing mechanisms.

**P1472 | BENCH**

Arrhythmias among young patients with multiple connective tissue abnormalities

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Purpose: Hereditary connective tissue diseases (Marfan syndrome, Ehlers Danlos syndrome, and etc.) are risk factors of arrhythmia and sudden cardiac death. We aimed to investigate the incidence arrhythmias among young patients with multiple connective tissue abnormalities but no signs and family history of known hereditary syndromes.

Methods: The study included 549 patients with connective tissue dysplasia (330 men, mean age 23.5±6.67). The main connective tissue abnormalities were signs of musculoskeletal system (n=549): abnormal curvature of the spine, flat feet, hyper-flexible joints, deformities of the anterior wall of the chest, dolichostenomelia and etc.), signs of cardiovascular system (n=409): prolapse of the mitral or aortic valves, aortic aneurysm, varicose veins and etc.), and signs of musculoskeletal system (n=119: primary pulmonary hypertension and etc.), and skin (n=169). Continuously monitoring heart activity (Holter monitor) was performed for all patients.

Results: Arrhythmias were detected in 69.95% of patients (n=384): episodes si- nus tachycardia (20.3%), inappropriate sinus tachycardia (1.9%), supraventricular tachycardia (3.83%), supraventricular tachycardia (3.83%), supraventricular arrhythmia (39.89%), vegetative sinus node dysfunction (0.73 per cent), the migration of the rhythm pacemaker (8.20%), ventricular extra-styptose (16.21%), supraventricular extrasystole (17.87%), paroxysmal atrial tachycardia (2.7%), atrioventricular node block (1.28%), sinoatrial node block (0.73%), infra-Hisian blocks (7.29%), WPW-syndrome (0.18%). Arrhythmia in 52.60% of cases combined with pathology of the heart valves, in 61.98% of cases (n=238; 95% CI 56.90-66.82) - with disorders of arteries and veins. Among patients with arrhythmias was significantly more men (n=253; 65.89%; p=17.27; p<0.000) and cases of aberrations of repolarization, diastolic dysfunction.

Conclusions: Arrhythmia increased the chance of recording aberrations of re- polarization (OR 4.39, p=0.000) and diastolic dysfunction (OR of 2.23, p=0.003). Factors increasing the likelihood of arrhythmias among young patients with multi- ple connective tissue abnormalities are (OR>2.00), pronounced manifestations of connective tissue dysplasia (OR 1.70, p=0.006), dispersion QTc- interval > 50 ms (OR 8.84, p=0.000), deviations from the normal cardiac index (OR 3.39, p=0.000).

**P1473 | BEDSIDE**

Insight into the pro-arrhythmic triggers in J wave syndrome: results of 15 year-follow up

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Purpose: Experimentally, hypokalemia increases the net repolarization current and enhances the transmural dispersion of repolarization in Brugada syndrome (BrS). On the other hand, we have recently reported recurrent ventricular fibrilla- tion (VF) related to hypokalemia in early repolarization syndrome (ERS). Taken together, we analyzed the importance of hypokalemia in ERS and BrS patients during long-term follow up.

Methods: From early 1999 to 2014, in our emergency department and after ex- cluding patients with chronic kidney diseases, serum potassium (S.K+) at time of resuscitation of 57 VF survivors was measured, including 24 patients with J- wave syndrome (11 ERS and 13 BrS patients) and 33 VF-survivors due organic heart disease (OHD).

Results: Immediately after resuscitation, S.K+ was significantly lower in J-group than in OHD group (3.1±0.9 mEq/L vs. 3.8±0.2 mEq/L; P=0.001). Interestingly, 3 pa- tients developed VF associated with hypokalemia shortly after starting oral steroid therapy for treatment of concomitant bronchial asthma, and they were free from any VF event after steroid discontinuation.

Furthermore, 3 patients with ERS had recurrent in-hospital electrical storms as- sociated with hypokalemia (S.K+: 2.65±0.05 mEq/L)and J-wave augmentation (J-amplitude 2.3±1.1 mm). Importantly, after successful resuscitation, they were kept on anti-mineralcorbicotics therapy with follow-up S.K+ of (3.72±0.24 mEq/L) and significant reduction in J- amplitude (0.91±0.5 mm, P=0.001) and free of VF episodes during follow up of 3.5–15 years.

Conclusion: In long-term follow up, hypokalemia has clearly added a substantial pro-arrhythmic effect in J-wave augmentation and VF mechanism in J-wave syn- drome and hence, strict prevention and treatment of even mild hypokalemia is crucial especially in patients with recurrent VF episodes.

**P1474 | BEDSIDE**

The rs3807989 G/A polymorphism in the CAV1 gene is associated with atrial fibrillation in Chinese Han populations

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Background: A recent meta-analysis of several genome wide association studies (GWASs) identified six new susceptibility single nucleotide polymorphisms (SNPs) for atrial fibrillation (AF) in individuals of European ancestry. We aimed to replicate the association between these SNPs and AF in a Chinese Han popula- tion.

Methods: We included a total of 597 cases with AF, and a control group consist- ing of 996 participants in absence of AF. The 6 SNPs were genotyped by using the middle-throughput iPLEX Sequenom MassARRAY platform. All statistical analy- ses were performed using STATA 12.0 software.

Results: Among the SNPs analyzed in the study, the SNP rs3807989 in the CAV1 gene on chromosome 7q31 was found to be significantly associated with AF (OR = 0.76; 95% CI. 0.64 – 0.90; P=0.001), with adjustment for gender and age in the additive model. When controlling for covariates of gender, age, hypertension, coronary artery disease (CAD), and diabetes, the relationship was still significant (OR = 0.75; 95% CI. 0.63 – 0.89; P=0.001).

Conclusion: In conclusion, we replicated the associations of SNPs identified by a GWAS with AF in Chinese Han populations. The study results showed that the SNP rs3807989 was significantly associated with AF. This finding may promote a better understanding of AF pathogenesis, risk prediction, and stratification of treatment strategy.

**CLINICAL ARRHYTHMOLOGY**

**P1476 | BEDSIDE**

Uninterrupted warfarin therapy has less bleeding as compared to heparin bridging in patients on chronic anticoagulation undergoing cardiac rhythm device implantation: a metaanalysis

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Introduction: Patients on chronic anticoagulation pose a complex clinical
showed that HEMOR(2)HAGES was significantly associated with hematoma occurrence in patients with uninterrupted OAC. These unanticipated findings suggest that score may represent a reliable predictor of hematoma occurrence among patients undergoing cardiac surgery.

**Conclusions:**

- Hemorrhagic and thromboembolic complications within 30 days after discharge were more frequent in the haemorrhagic group (2 of 13 patients) compared to the group without hemorrhagic complications (4 of 100 patients, p = 0.03).
- The rate of major bleedings was higher in the haemorrhagic group compared to the group without hemorrhagic complications (1 of 13 patients vs. 3 of 100 patients, p = 0.03).

**Methods:**

- Clinical trial evaluating the bleeding events in patients on anticoagulation undergoing cardiac rhythm devices implantation were considered. Studies were obtained using search words in Medline, PubMed, EMBASE, CINAHL, and Cochrane databases. The odds risk across all study groups was computed using Mantel-Haenszel random effects model. Results were calculated with 95% CI and were considered statistically significant if 2-sided alpha error was < 0.05.

**Results:**

- Eleven trials were included for analysis (n=795). Mean age and follow-up duration were 65.5 years and 4.1 weeks, respectively. The odds ratio of bleeding in patients on uninterrupted warfarin therapy compared to patients undergoing heparin bridging therapy was computed to be 0.35 (0.25, 0.47; p=0.00011 Picture 1).

**Conclusion:**

In patients undergoing cardiac rhythm devices implantation, uninterrupted warfarin therapy offers lower bleeding rates when compared to heparin bridging therapy.

P1477 | B E S I D E

**HEMOR(2)HAGES bleeding score predicts hematoma occurrence in patients with uninterrupted oral anticoagulation (OAC) undergoing cardiac device procedures**

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**Purpose:**

Uninterrupted oral anticoagulation (OAC) therapy during cardiac device procedures is associated with reduced hematoma formation as compared with bridging approach. The HASBLED score has previously shown to predict bleeding in patients undergoing cardiac and non cardiac procedures on bridging strategy. However, predictors of hematoma formation during uninterrupted OAC remain to be identified. The present study was designed to investigate whether the common bleeding risk scores [HASBLED, ATRIA and HEMOR(2)HAGES] predict hematoma occurrence in patients with uninterrupted OAC undergoing cardiac device procedures.

**Methods:**

Twenty-three patients (mean age 76.7±9 years, F:M=8:15) undergoing device procedures (11 replacements, 10 ex novo implants, 2 system/pocket revisions) during uninterrupted OAC were consecutively enrolled in the study. Main bleeding scores [HASBLED, ATRIA, HEMOR(2)HAGES] were calculated in all patients based on clinical, instrumental and laboratory parameters. Hematoma was clinically described as any suffusion or ecchymosis in the pocket area. All patients informed an signed consent before entering the study.

**Results:**

Five out of 23 patients (21.7%) developed pocket hematoma during the next 15 days after the procedure. Age (74±12 vs. 76±8, p=0.69) and gender (F:M 14:7 vs. 11:11, p=0.47) were comparable among patients with and without hematoma occurrence. By contrast, patients developing pocket hematoma displayed higher INR values (2.6±0.2 vs. 2.2±0.3, p=0.05). Among different bleeding scores, HEMOR(2)HAGES was significantly increased in patients with hematoma formation (2.6±0.9 vs. 1.3±0.8, p=0.01). Interestingly, linear regression analysis showed that HEMOR(2)HAGES was significantly associated with hematoma occurrence, regardless of gender and INR value (p=0.79, p=0.01).

**Conclusions:**

- Our pilot study indicates that HEMOR(2)HAGES bleeding score may represent a reliable predictor of hematoma occurrence among patients with uninterrupted OAC. These unanticipated findings suggest that HEMOR(2)HAGES score might be useful to warrant safer INR therapeutic ranges while minimizing bleeding risk in patients with uninterrupted OAC undergoing cardiac device procedures.

P1478 | B E S I D E

**Cost effectiveness of device surgery without interruption of oral anticoagulation: results from the bridge or continue warfarin for device surgery randomized controlled trial (Bruise control)**

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**Objective:**

The aim of present study was to assess the frequency of hemorrhagic and thromboembolic complications arising after permanent pacemaker implantation in patients receiving anticoagulant therapy with dabigatran etexilate.

**Methods:**

Prospective observational study included 16 patients with permanent or persistent atrial fibrillation (of whom 7 males) receiving dabigatran, who underwent primary pacemaker implantation between January 2013 and January 2014. The dabigatran group consisted of 16 patients with stabilised atrial fibrillation and underwent warfarin and underwent primary pacemaker implantation. Information about adverse events was collected during the initial hospitalization and over a period of following 30 days. Endpoints were defined as intraoperative bleeding; postoperative bleeding required additional surgical intervention or cancelling of anticoagulant treatment; requirement in plasma transfusion; incidence of hematomas that did not require surgery; thromboembolic complications of any localization.

**Results:**

Statistical analysis was performed using Statsistica 7.0 programs package; Fisher exact test was used to compare event frequencies in independent groups; comparisons of continuous variables were performed using Mann-Whitney test. Data is presented as “Me [25; 75]” [Median [interquartile range]].

**Conclusions:**

- The groups did not differ significantly by baseline parameters. All the pacemaker implantations were performed by standard protocol (with mean number of implanted leads of 1.2 in early group and 1.0 in late group). The intake of dabigatran and surgical intervention was 16 [12; 28] hours; interval before first dabigatran dose administration after pacemaker implantation ranged from 11 to 19 hours. In all patients receiving warfarin, the study was not interrupted. There were no major bleeding complications in early group patients. Postoperative period in dabigatran and warfarin groups. Hematoma that did not require surgical intervention occurred in 2 patients who took warfarin and in 1 patient in dabigatran group (p=0.48).

All patients completed the extended period of observation. There were no hemorrhagic or thromboembolic complications within 30 days after discharge both in groups receiving dabigatran and warfarin.

**Conclusions:**

- In patients receiving dabigatran, pacemaker implantation did not lead to increased frequency of bleeding or thrombotic events. Further studies are required to establish the safety of continued therapy with this anticoagulant in peripheroperic period.

P1479 | B E S I D E

**Permanent pacemaker implantation during anticoagulant treatment with dabigatran etexilate (single centre experience)**

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**Objective:**

The aim of this study was to assess the frequency of hemorrhagic and thromboembolic complications arising after permanent pacemaker implantation in patients receiving dabigatran etexilate.

**Methods:**

Prospective observational study included 16 patients with permanent or persistent atrial fibrillation (of whom 7 males) receiving dabigatran, who underwent primary pacemaker implantation between January 2013 and January 2014. The dabigatran group consisted of 16 patients with stabilised atrial fibrillation and underwent warfarin and underwent primary pacemaker implantation. Information about adverse events was collected during the initial hospitalization and over a period of following 30 days. Endpoints were defined as intraoperative bleeding; postoperative bleeding required additional surgical intervention or cancelling of anticoagulant treatment; requirement in plasma transfusion; incidence of hematomas that did not require surgery; thromboembolic complications of any localization.

**Results:**

Statistical analysis was performed using Statsistica 7.0 programs package; Fisher exact test was used to compare event frequencies in independent groups; comparisons of continuous variables were performed using Mann-Whitney test. Data is presented as “Me [25; 75]” [Median [interquartile range]].

**Conclusions:**

- The groups did not differ significantly by baseline parameters. All the pacemaker implantations were performed by standard protocol (with mean number of implanted leads of 1.2 in early group and 1.0 in late group). The intake of dabigatran and surgical intervention was 16 [12; 28] hours; interval before first dabigatran dose administration after pacemaker implantation ranged from 11 to 19 hours. In all patients receiving warfarin, the study was not interrupted. There were no major bleeding complications in early group patients. Postoperative period in dabigatran and warfarin groups. Hematoma that did not require surgical intervention occurred in 2 patients who took warfarin and in 1 patient in dabigatran group (p=0.48).

All patients completed the extended period of observation. There were no hemorrhagic or thromboembolic complications within 30 days after discharge both in groups receiving dabigatran and warfarin.

**Conclusions:**

- In patients receiving dabigatran, pacemaker implantation did not lead to increased frequency of bleeding or thrombotic events. Further studies are required to establish the safety of continued therapy with this anticoagulant in peripheroperic period.
P1480 | BEDSIDE
Higher mortality seen in patients with frequent premature atrial contractions

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Purpose: Frequent premature atrial complexes (fPACs) have been reported as a risk factor for Atrial Fibrillation (AF). Some studies have linked fPACs to high mortality. More work is needed to establish this relationship.

Methods: We analyzed Holter recordings obtained between 2000 and 2010 of 1357 patients free of AF at baseline. Holter groups with fPAC (>100/day) and infrequent PACs (<100/day) were compared. Electronic medical records and EKGs were reviewed to ascertain baseline characteristics as well as occurrence of AF and death during median follow-up of 7.5 yrs. Logistic regression and Kaplan-Meier analyses were performed.

Results: Mean age was 64 yrs with 93% men. Mean BMI, A1c, left atrial size and average HR were 31.24 kg/m², 6.42%, 42.56 mm and 73 bpm, respectively. 37.31% of patients with fPACs died during follow-up as compared to 18.87% in non-fPAC group. After adjusting for demographics, medication use, co-morbidities, lab and echo findings, multivariate regression analyses confirmed fPACs to be independently associated with higher incidence of death (OR 1.44, 95%CI 1.07-1.92, P=0.015). Furthermore, mortality rates in patients with +fPAC/+AF, -fPAC/+AF, +fPAC/-AF and -fPAC/-AF were 48.11%, 36.73%, 34.3% and 17.8% respectively (p<0.0001).

Conclusions: Patients with fPACs (>100/day) have higher all-cause mortality, especially when they develop subsequent AF.

P1481 | BEDSIDE
Anti-arrhythmic drugs did not reduce progression from paroxysmal to sustained atrial fibrillation: from the Fushimi AF Registry

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Purpose: Atrial fibrillation (AF) increases the risks of thromboembolism and death, and the prevalence of AF is increasing significantly (reportedly, 0.6% of 457 paroxysmal AF patients (32.7%) were prescribed AAD at baseline. 3 patients for Ia (5.6%), 2 patients for Ib (11.8%), 16 patients for Ic (5.0%), 2 patients for amiodarone (15.4%) and 3 patients for bepridil (8.8%). Progression of AF occurred in 25 patients with single AAD (5.8%) and 2 patients with multiple AADs (6.9%).

Conclusion: 5.7% of paroxysmal AF patients progressed to sustained AF in a year. Any class of AAD did not reduce progression from paroxysmal to sustained AF, during one-year follow-up of the Fushimi AF Registry in Japanese AF patients.

P1482 | BEDSIDE
Temporal changes in spatial characteristics of scar tissue in an experimental model of acute myocardial infarction: an MRI study

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Background: Spatial characteristics of scar tissue including total extent of heterogeneous tissue (HT) and intrascar corridors of HT are related to cardiac mortality. However, little is known concerning evolution of scar architecture during the first months after acute myocardial infarction (AMI).

Methods: A transmural anterior AMI was created in 12 pigs. Myocardial scar was characterized 5 weeks and 18 weeks later with gadolinium cEMRI. End-diastolic and end-systolic left ventricular volumes (EDV and ESV), left ventricular mass and necrotic mass were quantified with QMass 7.2® MEDIS. The ventricular wall was divided in 2 layers and the average of the subendocardial and subepicardial signal intensity (SI) was measured over 3D endocardial and epicardial shells. The SI was color coded, thus defining tissue areas: 1) healthy tissue defined by SI< SI peak in normal myocardium, 2) core scar defined by SI greater than minimal SI in core scar and 3) heterogeneous tissue (HT) in between these extremes. A SI channel was defined as a corridor of HT differentiated by a lower SI from the surrounding scar.

Results: Mean EDV and ESV at 5 weeks after AMI were 114±13 cc and 77±13 cc, with a mean ejection fraction of 29±9%. Mean increase of EDV and ESV at 18 weeks was 49±15 cc and 31±17 cc. Between 5 weeks and 18 weeks, mean reduction of endocardial and epicardial scar area was 5±13 cm² and 3±15 cm². At 5 weeks, 10 endocardial and 16 epicardial SI channels were observed. At 18 weeks, 20 endocardial and 18 epicardial SI channels were identified.

Conclusions: Spatial characteristics and architecture of scar change over time in the first months after AMI. A better knowledge of patterns of evolution of scar could be relevant for risk stratification in ischemic heart disease.
**Conclusion:** In the patients with structurally normal heart, IVCD was associated with future development of atrial fibrillation. However complete atrioventricular block, heart failure, sick sinus syndrome and all-cause mortality were not increased in the patients with IVCD.

**P1484 | BEDSIDE**

The prognostic value of ST-segment elevation in lead aVR in patients with idiopathic pulmonary arterial hypertension

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**Background and aims:** We aimed to investigate the relation between the presence of ST-segment elevation in lead aVR in electrocardiography with the severity of disease assessed with clinical, hemodynamic, and neurohormonal parameters in patients with Idiopathic Pulmonary Arterial Hypertension (IPAH).

**Methods:** The study group comprised 28 patients with IPAH. Six-Minute Walking Distance (6MWD), plasma Brain Natriuretic Peptide (BNP), history of hospitalizations secondary to acute worsening states and needed to escalate the treatment were used to assess the clinical, hemodynamic, and neurohormonal status of patients.

**Results:** There were no significant differences between distinguished groups in terms of: age, disease duration, hemoglobin levels, oxygen saturation, baseline function for NYHA class, 6MWD, cardiac output, BNP, pulmonary artery systolic pressure, right atrial pressure, pulmonary vascular resistance. Whereas patients with aVR-ST elevation had a higher heart rate (84±13 vs 67±5, p = 0.007) as compared to those not. Mean follow-up period was 27±3 months after diagnosis. During this period patients with the presence of ST-segment elevation in lead aVR had higher clinical worsening states (acute deterioration (16 vs 5, p < 0.05) and more needed to escalate the PAH specific therapy (11 vs 3, p < 0.05) and higher mortality (5 vs 1, p < 0.05) compared to those not.

**Conclusions:** IPAH patients with the presence of ST-segment elevation in lead aVR in ECG had significantly worse survival in reference to those with not. The observed presented above establish presence of aVR-ST elevation may indicate the functional impairment and may also have a prognostic potential enabling the identification of patients with higher risk of unfavourable disease course during follow-up period.

**P1485 | BEDSIDE**

Do patients really wear their wearable cardioverter-defibrillator?

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**Introduction:** Indications for the use of wearable cardioverter-defibrillator (WCD) expanded over the last years. Nevertheless, only little is known about the patient compliance with the treatment with a WCD.

**Material and methods:** We collected the data of all patients treated with a WCD between 2009 and 2013 in our institute and analyzed them with special regard to the wearing discipline.

**Results:** 26 patients (21 male, 5 female, mean age 62.4±13.7 years [range 28–83 years]) were treated with a WCD over 1509.7±332.3 hours [range 180.5–3063.93 hours]. There was no appropriate but one inappropriate shock and half of all patients received an implantable cardioverter – defibrillator (ICD) during follow-up. The WCD was worn 23.2±1.9 hours each day [range 13.9–24.0 hours].

**Discussion and conclusion:** The patient's compliance with the treatment with a WCD was very good. The treatment discipline might be influenced by the choice of the right patient, the choice of the right VT threshold to avoid inappropriate shocks as well as the regular controlling of the wearing discipline.

**DIAGNOSIS OF ARHYTHMIA**

**P1487 | BEDSIDE**

Diagnostic approach of idiopathic ventricular fibrillation: results from the FIVI-Gen study

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**Background and objectives:** Idiopathic Ventricular Fibrillation (IVF) is a rare entity that might be due to subclinical underlying cardiomyopathies and channelopathies of genetic origin. We aim to assess the diagnostic yield of a novel systematic protocol in patients with IVF.

**Methods:** IVF was defined as sustained VF episode which required external defibrillation, and with no pathological findings in basal electrocardiogram (EKG), echocardiogram, and coronary angiography. The diagnostic protocol consisted of three sequential steps: 1.- pharmacological tests with epinephrine and flecainide; 2.- first and second-degree relative’s assessment with EKG and echocardiogram and 3.- genetic testing with next-generation sequencing method including 126 genes for cardiomyopathies and channelopathies.

**Results:** Thirty-five patients (60% males, mean age 39.3±14.5 years) from 9 Spanish centres were assessed. Final diagnosis was obtained in 19 probands/families (54.2%). The most prevalent underlying etiology were Cathoco-laminergic Polymorphic Ventricular Tachycardia (20%), Brugada Syndrome (17.1%) and Long QT syndrome (8%). The way to reach the diagnosis and a summary of the results are shown in figure 1. Relevant, but un conclusive findings, were observed in 10 other cases (28.5%), not completely fulfilling current diagnostic criteria for the specific disease. Among these cases we found a possible arrhythmogenic right ventricular cardiomyopathy, two possible hypertrophic cardiomyopathy patients and a lamin A/C mutation with no clear phenotype in other case.

**Conclusions:** Cardiac channelopathies are the most prevalent underlying diagnosis in IVF. This novel systematic protocol achieves a definitive diagnosis in more than a half of previously “idiopathic” VF episodes.

**P1488 | BENCH**

Steepening of the slope of QT interval restitution is a risk factor for drug-induced arrhythmias

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**Introduction:** An excessively prolonged, rate-corrected QT interval (QTc) is a clinical marker of increased risk of arrhythmic sudden death. Similarly, a steep ventricular restitution curve slope has been associated with increased risk of ventricular arrhythmias (VA). In experimental studies QT interval prolonging drugs consistently steepen ventricular restitution slopes constructed by recording electrogaphic or action potentials. In vivo, dependence of QT on diastolic interval (DI) has been assessed via 24-h Holter recording, a method limited to spontaneous rhythms that does not analyze QT/DI slope. We used a steady state ventricular pacing (VP) protocol to study doflidilide (DOF) effects on QT restitution, hypothesizing that prolonged regularization would be associated with steeper restitution slopes.

**Methods:** We performed VP in 7 anesthetized dogs at cycle lengths (CL) 5-10% < sinus CL. VP consisted of abrupt shortening of basic CL (BCL) for 1 min followed by a return to BCL. We constructed QT restitution curves using the last 10 beats preceding a return to BCL, at which time steady-state QT shortening had occurred. DOF was administered during sinus rhythm to obtain >25% QTc increase (Bazett formula).

**Results:** DOF prolonged QTc from 378±5 to 559±30 (p<0.05) and sinus CL from

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Identification of the arrhythmogenic substrate in acute phase of STEMI


Purpose: A 3D reconstruction of the contrast enhanced-cardiac magnetic resonance (ce-CMR) allows visualization of scar and border zone (BZ) channels. BZ channels have been identified as critical isthmuses of ventricular tachycardia. We hypothesized that this arrhythmogenic substrate could be identified in the acute phase of a ST elevation myocardial infarction (STEMI).

Methods: Consecutive patients with STEMI and primary percutaneous coronary intervention were included. A 3D high-resolution 3T ce-CMR was obtained within the first 6 days and at 6 month. LV volumes and left ventricular ejection fraction (LVEF) were measured. The LV wall was segmented and characterized using a pixel signal intensity algorithm at 10 myocardial layers. A 3D color-coded shell map was obtained for each layer to depict the scar core and BZ distribution. The presence/characteristics of BZ channels were registered for each layer in both studies. Myocardial scar was classified as arrhythmogenic if BZ channels were present.

Results: 40 patients (32 male, 57.7±10.9 years) were included. LVEF improved from 48.4%±9.7 to 52.3%±10.9 (p=0.001) at 6 months and LV end diastolic volume tended to increase from 161.8±39.4 ml to 170.4±54.8 ml (p=0.128). 44 BZ channels were present baseline and 41 of them (93.1%) were present in the same segment/orientation at 6 days and 6 months (Figure 1). 26 (65%) patients were classified as having arrhythmogenic scar at baseline and 24 (92.3%) persisted at 6 months. Two (5%) patients had spontaneous sustained ventricular arrhythmias during follow-up and both had BZ channels in the acute phase.

Conclusions: Ce-CMR can identify BZ channels in acute phase of STEMI that persist visible in the healed infarction, suggesting its usefulness for sudden cardiac death risk stratification.

Systolic of early detection and active management of supraventricular arrhythmia with remote monitoring: The SETAM trial

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Purpose: Atrial fibrillation is the most commonly encountered sustained cardiac arrhythmia in medical practice and it is often associated with conduction disorders. Biotronik home monitoring (HM) technology provides relevant notifications for detection of supra-ventricular arrhythmias (SVA). The SETAM randomized, multicenter trial assessed the impact of HM on detection and treatment of SVA.

Method: Patients implanted with a dual chamber pacemaker were enrolled in the study at hospital discharge if they had a sinus rhythm at enrollment, no antirhythmic, anticoagulant or dual-antiplatelet therapy, and if they had a CHA2DS2-VASc score for stroke risk of 2 or more. The patients were randomly assigned to an active group, followed by HM, or a control group without HM surveillance. The time from enrollment to the management of SVA was compared between the two groups.

Results: A total of 595 patients (mean age = 79±8 y.o., 63% male, mean CHA2DS2-VASc score = 3.7±1.2) were followed during 12.8±3.3 months. There was no difference in the baseline clinical characteristics between the two groups. The most prevalent concomitant co-morbidities were hypertension (82% patients), diabetes (29%) and vascular disease (24%). Implantation indications were atrio-ventricular blocks in 77% of patients, sinus node disease in 20% and conduction disorders or others in 3%.

The global SVA incidence was 25% (29% in the active group vs 22% in the control group, p=ns). A therapy (drugs or ablation) was instigated in 47/291 patients (16%) in the active group versus 44/304 patients (14%) in the control group (p=ns). The treatment strategy was the same between the groups; anticoagulation was initiated in the majority of patients (75%), antiarrhythmic drugs in 49% of patients.

The median time from enrollment to the first therapy for SVA was 109 [44; 211] days in the active group versus 210 [66; 370] days in the control group, representing a median gain of 101-days in SVA management (48% reduction, p=0.01). In the active group, 93% of the notifications transmitted by HM were appropriate
Introduction: Catheter ablation of ventricular arrhythmia (VA) has been greatly facilitated by 3D image integration. We described the combination of SPEC T images of myocardial perfusion and the distribution of the sympathetic activity which is projected on the 3D endo- and epicardial surface of the left ventricle from contrast computed tomography (cCT).

Methods: Five patients (3 males, median age 63 yrs) scheduled for VA ablation were studied. Three had ischaemic heart disease, 1 hypertrophic cardiomyopathy, 1 dilated cardiomyopathy + LV normo-compaction, 1 bronchiectasis. Three patients had implanted ICD. All patients underwent cCT and dual-tracer radionuclide imaging with 123I-methiodobenzylguanidine (mIBG) for sympathetic innervation and 99mTc-methoxyisobutylisonitrile (MIBI) for viability using a solid-state camera (DSE PCT, Spectrum Dynamics). Regions of mismatch between mIBG and MIBI uptake were identified. The merged images were imported into an anatomical mapping system (CARTO, Biosense Webster) and were available during VA ablation.

Results: All imaging studies were performed without complication. There was good agreement between the voltage amplitude map and myocardial viability except in areas that were inaccessible to the catheter. Location and region of mismatch varied between the substrates and were not necessarily related to scars. A 2 months follow-up demonstrated no recurrence of sustained VA and no ICD interventions.

Conclusion: The combination of anatomical and functional information on myocardial viability and innervation provides a novel type of “road map” for VA ablation. Superimposition of this multiplexed information allows for the first time to localize the region of mismatch which may be pre-arrhythmogenic. Larger prospective studies are warranted.

P1492 | BEDSIDE
Identification of the underlying substrate in patients with ventricular arrhythmias: imaging the mismatch of perfusion and sympathetic innervation
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Results: The median follow-up period was 108 (67.5; 120.0) months. After 10 years since the first enrolled patient cardiac conductions have been registered in (87.8%) OSA subjects [9 cases of AV block, SA block was registered in 8 subjects; there was a combination of AV and SA conduction disturbances in 1 patient; four of them required pacemaker implantation] while none from control group developed conduction disorder (z=5.4; 16; p=0.015). The multiple Cox-regression analysis demonstrated that the following factors were associated with the conduction disorder development: AHI (p=0.007), and beta-blocker use (p=0.047). BMI had a borderline significance (p=0.07). When apnea duration was excluded in the model it showed to be a significant predictor (p=0.002), while AHI became non-significant (p=0.32).

Conclusions: Our data suggest that OSA is associated with the development of cardiac conduction disorder in hypertensive patients, and the duration of apnea emerges crucial. Suggesting the role of autonomic disbalance the underlying mechanisms require further investigation.

P1493 | BEDSIDE
Arrhythmias in patients with chronic kidney disease – data with implanted loop recorders
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Conclusion: The underlying combination of sympathetic and cardiac mechanisms require further investigation.

P1494 | SPOTLIGHT
New criteria during right ventricular apical entrainment to differentiate between AVNRT and ORT
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Purpose: Patients with severe chronic kidney disease are known to have high prevalence of different arrhythmias. However, previous studies have lacked technological capacity to adequately detect rhythm disturbances over periods of months or years. This is the first study to use subcutaneously implanted loop recorders to gather reliable long-term arrhythmia data from this patient group. Methods: The present preliminary data is based on 27 patients (62±7.7 years [mean±SD], range 45 to 74 years, 19 men) with more than 2 months of follow-up; the patient pool is continuously expanding. The main kidney diseases were diabetic nephropathy (11 patients), polycystic kidney disease (6) and chronic glomerulonephritis (5). All the patients had stage 4 or 5 renal failure. One patient was in the pre-dialysis stage, two received peritoneal dialysis, while the rest were treated with hemodialysis. The median time since the start of the dialysis was 2.0 years. Six patients (22%) were known to have some manifestation of atrial fibrillation (AF) prior to the implantation of the loop recorder, 3 chronic and 3 paroxysmal AF; being in line with published data.

Results: During the follow-up of 16±6 months, 17 (63%) patients had documented episodes of AF. Four patients (15%) had bouts of non-sustained ventricular tachycardia; this fact was unknown before the loop recorder data. Two patients had Bradycardia, revealed by the device, necessitating a pacemaker. Five patients died, two of them due to ventricular tachyarrhythmia.

Conclusions: Prevalence of several types of arrhythmia, documented with loop recorders, is essentially higher than previously thought in patients with severe kidney disease. Particularly, occurrence of AF is over twice as common as given in the literature. These findings, if confirmed with the accumulating number of patients in this investigator-initiated study, may have marked clinical implications regarding pharmaceutical as well as device therapy.
**P1498 | BEDSIDE**

Cardiovascular magnetic resonance findings and the value of anticardiac antibodies in patients with inflammatory dilated cardiomyopathy and conduction disturbances with structurally normal heart

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**Purpose:** To compare the persistence of inflammation according to endomyocardial biopsy (EMB) and cardiovascular magnetic resonance (CMR) and the level of circulating autoantibodies in inflammatory dilated cardiomyopathy (DCMi) patients (pts) and pts with conduction disturbances and structurally normal heart (CD).

**Methods:** 22 pts with CD and structurally normal heart (8 male, mean age 39.3±11.0) and 22 pts with DCMi (10 male, mean age 40.5±10.5) underwent Holter ECG monitoring with subsequent CMR with assessment of myocardial edema (ME), early gadolinium enhancement (EGE) and late gadolinium enhancement (LGE). In serum of all pts persistence of autoantibodies to beta-taladnergic receptor (p1-Abbs) and M2 muscarinic receptor (M2-Abbs) was evaluated. In pts with DCMi endomyocardial biopsy (EMB) was performed.

**Results:** EMB revealed active inflammation in 14 (60.9%) of DCMi pts, that was proved by CMR only in 7 of them (<,2 criteria). The most frequent finding in these pts was LGE – in 12 pts (54.5%) (the volume of affected myocardium was 22.8 [16.95;51.1] cm3), ME was found in 8 pts (36.4%), sighs of EGE in 7 pts (31.8%). 17 (77%) of DCMi pts have shown elevated level of IgG1-Abbs. LG was characterized by higher number of ventricle premature complexes (VPC) (3643 [255;8500] vs 65 [64;2403]) p=0.04 and higher level of p1-Abbs IgG (1.16 [0.71;2.05] vs 0.69 [0.54;0.93], p=0.019). The amount of p1-Abbs correlated with number of non-sustained ventricular tachycardia (VT), total amount of VPC, and volume of myocardium with LGE (r=0.71, 0.47, 0.61 respectively) in DCMi pts. None of CD pts revealed LGE at CMR. 4 (18.2%) of them had ME, 7 (31.8%) were EGE positive, 2 (9.1%) of them had positive CMR criteria.

**Conclusion:** 77% DCMi pts revealed enhanced level of IgG to p1-Abbs which correlates with total amount of VPC, number of VT and volume of myocardium with LGE. IgM to M2-Abbs revealed the best diagnostic value in detection of inflammatory myocardial damage in EMB data (S=0.889) in DCMi pts.

**P1499 | BEDSIDE**

B cells within human stenotic aortic valves are associated with the severity of aortic stenosis: relation to inflammatory infiltration and calcification within the leaflets

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**Purpose:** Recent studies highlighted the importance of macrophage-B cell bidirectional interaction in the pathogenesis of atherosclerosis, which is to some extent similar to aortic stenosis (AS). Macrophage-derived BAFF protein drives B cell activation, and probably, B cells in turn regulate macrophage function, impairing their ability to phagocytose. A role of B cells in AS is largely unknown. The aim of this study was to investigate the in loco presence of B cells within aortic valve leaflets and to determine its interactions with AS severity.

**Methods:** 37 patients with dominant AS undergoing aortic valve replacement were studied (age, 59.7±10.6 years; mean gradient, 41.23±12.54 mmHg). In direct immunohistochemistry was performed on decalcified valve leaflets using double staining showed that 27±13.5% of B cells express receptor BAFF-R. There were positive correlations between the number of B cells and macrophages (r=0.45, p=0.018) and between macrophages and B cells-associated BAFF-R expression (r=0.66, p=0.002). Moreover, the number of B cells showed a positive correlation with the degree of valve calcification (r=0.41, p=0.039) and with maximum (r=0.63, p=0.02), but not mean transvalvular gradient, and tended to correlate with aortic valve area (r=0.45, p=0.049). There were no statistically significant correlations between B cells within the leaflets and plasma CRP or fibrinogen.

**Conclusions:** B cells are present within aortic valve leaflets in increasing numbers when the severity of AS and valve calcification augment, which supports the concept that dysregulated immune mechanisms like in atherosclerotic plaques may play a significant role in the pathogenesis of AS. We postulate that the interaction between B cells and macrophages, through BAFF-R receptor within aortic valve leaflets may impair the clearance of apoptotic bodies, which in turn may enhance valvular calcification and potentiate the progression of AS.

**P1500 | BENCH**

Calumenin is involved in early and late stages of arterial calcification

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**Purpose:** Calumenin (CALU) is a small extracellular zinc metalloproteinase that inhibits bone morphogenetic protein-2 (BMP-2) is a major regulator of calcification and miR-141 is a repressor of the osteogenesis mediated by BMP-2. Recently, Yanagawa et al demonstrated a downregulation of miRNA-141 expression in patients with bicuspid aortic valve, a known condition of high risk of calcification. Our hypothesis is that plasmatic levels of miR-141 could be a plasma biomarker for valvular calcification risk.

**Methods:** We have enrolled 62 patients undergoing aortic valve replacement for calcific aortic stenosis without coronary disease or another valvular pathology, from March 2012 to December 2013. We obtained valvular leaflets at surgery and plasma samples. Total RNA was isolated from plasma and tissue, and miR-141 levels were determined by quantitative RT-PCR (qPCR). Levels of α-smooth muscle, or 4.5S RNA when appropriated, were used to normalize samples.

**Conclusions:** Low levels of miR-141 and high plasma levels of calcification-related markers were found in patients with AS. However, there is a clear correlation between miR-141 and glomerular filtration rate (p=0.028) and treatment with warfarin (0.047). In addition, plasma levels of miR-141 had a trend to be lowered in patients with severe left ventricular hyper trophy and bicuspid valve, although without statistical significance.

**P1499 | BENCH**

MiR-141: a novel plasma biomarker for calcific aortic stenosis?

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**Purpose:** Calcific aortic stenosis (CAS) is a dystrophic calcification process whose pathophysiology is in relation with osteogenic proteins. Bone morphogenetic protein-2 (BMP-2) is a major regulator of calcification and miR-141 is a repressor of the osteogenesis mediated by BMP-2. Recently, Yanagawa et al demonstrated a downregulation of miRNA-141 expression in patients with bicuspid aortic valve, a known condition of high risk of calcification. Our hypothesis is that plasmatic levels of miR-141 could be a plasma biomarker for valvular calcification risk.

**Methods:** We have enrolled 62 patients undergoing aortic valve replacement for calcific aortic stenosis without coronary disease or another valvular pathology, from March 2012 to December 2013. We obtained valvular leaflets at surgery and plasma samples. Total RNA was isolated from plasma and tissue, and miR-141 levels were determined by quantitative RT-PCR (qPCR). Levels of α-smooth muscle, or 4.5S RNA when appropriated, were used to normalize samples.

**Conclusions:** miR-141 was almost undetectable in plasma of patients and, therefore, this miRNA would not be useful as a biomarker. On the other hand, miR-141 was associated with left ventricular hypertrophy, renal function and warfarin treatment. Thus, our study is open to confirm if miR-141 is a principal key in valvular calcification process and could be a novel therapeutic and preventive strategy for calcific aortic stenosis.
P1501 | BENCH
Moderate diet restriction can reverse alterations of cardiac function induced by postnatal overfeeding in mice
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Postnatal overfeeding (OF) in rodents induces a permanent moderate increase in body weight, metabolic disorders and progressive alterations of cardiac function. Our aim was to determine whether moderate diet restriction could restore cardiac function in mature overfed mice.
Immediately after birth, litters of C57BL/6e mice were either maintained at nine (normal-fed group, NF), or reduced to three in order to induce OF. At weaning, mice of both groups received a standard diet ad libitum (AL). At 6 months of age, half of the OF mice were assigned to a moderate 20% calorie restriction (CR, OF-CR) for one month, while NF and the other half of the OF mice continued to eat ad libitum (NF-AL, OF-AL). Cardiac function was followed using echocardiography and, at 7 months, the sensitivity to ischemia-reperfusion injury was evaluated in isolated perfused hearts.
Six-month-old OF mice weighed 22.5% more than NF mice. Left ventricular fractional shortening (LVFS) and ejection fraction (LVEF) were decreased in OF mice (25.5% vs. 30.5% for LVFS; 50% vs. 58% for LVEF, p < 0.05). Left ventricular internal diameter in diastole (LVIDd) and systole (LVIDs) were significantly greater in OF than NF mice. One month of moderate CR normalized body weight in OF-CR compared with OF-AL (31.1 vs. 37.4 g, p < 0.001). Moreover, LVEF was greater in OF-CR than OF-AL (61% vs. 52%, p < 0.05) and became comparable to that in NF-AL. LVIDd and LVIDs were also normalized in OF-CR. Ex vivo, after 30 min of global ischemia, hearts isolated from OF-CR mice showed better functional recovery than those of the two other groups.
Our study suggests that short-term moderate diet restriction could normalize body weight gain induced by postnatal OF and, interestingly, could reverse alterations of cardiac function and susceptibility to myocardial ischemia-reperfusion injury in OF.

P1502 | BENCH
Aggregation levels by PEAR1 genotype
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Pearson correlation analysis. The expression levels of adiponectin, PGC-1α, and ESRRG were decreased in 3T3-L1 cells overexpressing inhibitors of miRNA-378. Luminiscence activity in HEK 293 cells expressing a renilla-lucerase-adiponectin-3'UTR sequence was significantly inhibited by overexpressing mimics of miRNA-378, and the decrease was reversed by adding inhibitors of miRNA-378, indicating that post-transcriptional activity of the adiponectin 3'UTR was regulated via the miRNA-378-binding site (in vivo analysis). In conclusion, we found that intracellular levels of miRNA-378 were crucial for expression of adiponectin and that they could modulate adiponectin levels posttranscriptionally via the 3'UTR sequence-binding site.
Conclusion: For our study, we determined that platelet aggregation across platelet function tests and agonists (Figure). Carrying the PEAR1 A-allele was also associated with increased platelet activation (p<0.05), but not with cyclooxygenase-1 activity. Platelet aggregation was unaffected by the other SNPs analyzed.

P1503 | BENCH
Moderate post-transcriptional regulation of adiponectin by miRNA-378 in adipose tissue: a novel mechanism for hypoadiponecminemia
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Background: It is well known that hypoadiponecminemia is associated with high prevalence of cardiovascular events, but the mechanisms for hypoadiponecminemia are largely unknown. MicroRNAs (miRNAs), small non-coding RNAs that regulate gene expression post-transcriptionally, are involved in biological processes, including obesity and insulin resistance. We evaluated whether the miRNA-378 pathway is involved in adiponectin gene transcription.
Methods and results: First, we determined a putative target site for miRNA-3 in the 3' untranslated region (3'UTR) of the adiponectin gene by bioinformatic analysis. The expression levels of adiponectin, PGC-1α, and ESRRG were decreased in 3T3-L1 cells overexpressing inhibitors of miRNA-378. Luminiscence activity in HEK 293 cells expressing a renilla-lucerase-adiponectin-3'UTR sequence was significantly inhibited by overexpressing mimics of miRNA-378, and the decrease was reversed by adding inhibitors of miRNA-378, indicating that post-transcriptional activity of the adiponectin 3'UTR was regulated via the miRNA-378-binding site (in vivo analysis). In conclusion, we found that intracellular levels of miRNA-378 were crucial for expression of adiponectin and that they could modulate adiponectin levels posttranscriptionally via the 3'UTR sequence-binding site.
Conclusion: For our study, we determined that platelet aggregation across platelet function tests and agonists (Figure). Carrying the PEAR1 A-allele was also associated with increased platelet activation (p<0.05), but not with cyclooxygenase-1 activity. Platelet aggregation was unaffected by the other SNPs analyzed.

P1504 | BEDSIDE
Cerebral perfusion in patients with metabolic syndrome: relationship with endothelial dysfunction and cognitive disorders
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Purpose: To estimate role of endothelial dysfunction in development cerebral per- fusion disturbance and cognitive disorders in patients with metabolic syndrome (MetS). Methods: The study involved 52 patients (mean age 52±5) with MetS. Fifteen healthy volunteers were investigated as control group. All patients were investi- gated by perfusion brain SPECT with 99mTc-HMPAO and comprehensive neu- rological testing. Endothelial function was assessed by flow-mediated dilatation in brachial artery by vascular Doppler after pneumatic tourniquet stress at forearm according to D.Celermajer. Brain SPECT slices were divided into 14 symmetrical (right and left) regions of interest per patients: inferior and superior frontal lobes, temporal, anterior and posterior parietal, occipital lobes and cere- bellar hemispheres. Regional cerebral blood flow (rCBF) (ml/100g/min) in these regions was calculated.
Results: The results of Brain SPECT showed that cerebral perfusion was signifi- cantly decreased in regions of MetS patients in comparison with control group. The regional cerebral blood flow in patients with metabolic syndrome in decrease on 7.3% (p<0.003), 6% (p<0.028), 5.9% (p<0.024) was revealed in right and left anterior parietal cortex, in right posterior parietal region correspondingly, as well as with decrease on 8.3% (p<0.007), 6.6% (p<0.009) and 5% (p<0.041) in right superior frontal cortex, in right temporal and occipital regions, correspondingly, in comparison with control patients. Cognitive dysfunction was detected in 90% MetS patients. The flow-dependent vasodilatation in MetS patients was decrease on 14.3% in comparison with control group (p<0.021). In addition in 32 (61%) from 52 MetS patients was observed inadequate change of brachial artery diameter in reactive hyperemia peak, in 11 (22%) patients registered constricted response on reactive hyperemia and only in 9 (17%) patients detected normal response. Relation- ship between rCBF, cognitive function and indices of endothelial dysfunction was found. Significant correlation was shown between flow-dependent dilatation in MetS patients and rCBF in left superior frontal region (R2=0.126; p=0.023). The brachial artery diameter in phase of reactive hyperemia positive correlated with rCBF in left superior frontal cortex, temporal and right anterior parietal regions (R2=0.277, p=0.006, R2=0.272, p=0.026, respectively), as well as with visualognition function (R2=0.415; p<0.009).
Conclusion: Deterioration of cognitive functions in MetS patients was associated with endothelial dysfunction and brain perfusion decreasing.
P1505 | BENCH
Uptregulation of the vanilloid 2 receptor channel in HL-1 cells exposed to hypoxia may induce rapid cell death
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Purpose: A new super-family of channels that may have a role in cardiac calcium homeostasis has recently been described. These are non-selective and non-voltage-gated transient receptor potential (TRP) channels; most of them are permeable for Ca²⁺ and gated by diverse stimuli. Published evidence dictates that dilated cardiomyopathy is associated with an accumulation of the TRP vanilloid 2 (TRPV2) channel in cardiomyocytes in various heart failure animal models as well as in patients. We sought to assess whether TRPV2 overexpression may affect cardiomyocyte cell viability following myocardial infarction.
Methods: Murine HL-1 cardiomyoid cells were exposed to hypoxic conditions for 18 hours. TRPV2 levels on the cell membrane were tested by flow cytometry using an anti-TRPV2 antibody. Cellular viability was assessed by Annexin V-FITC-PI assay followed by flow cytometry analysis. The direct effect of TRPV2 on cell viability was studied by introducing a TRPV2 or scramble siRNA to the cells prior to the exposure to hypoxia.
Results: TRPV2 expression on the cell membrane was elevated by 60% upon exposure to hypoxia. The upregulation of this channel protein was correlated with a significant reduction in cellular viability (77.8 ± 4.3 percent viability in normoxic vs. hypoxic conditions). Interestingly, transient transfection with a TRPV2 siRNA inhibited the cell death observed in the scramble-siRNA or untransfected HL-1 cells under hypoxia. The viability of HL-1 cells grown under normoxic conditions was not affected by the siRNA.
Conclusion: TRPV2 may play an important role in mediating cardiomyocyte cell death following myocardial infarction. These data point to a potential novel therapeutic target for cardiomyocyte cell loss occurring shortly after an acute MI.

P1506 | BENCH
Prognostic value of plasma LMP in diabetic patients with acute coronary syndrome
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Purpose: Leukocyte-derived microparticle (LMP), originating from activated or apoptotic leukocytes, is increased in patients with cardiovascular risk factors. We evaluated whether LMP is an independent marker for cardiovascular events in diabetic patients with acute coronary syndrome (ACS), and discussed the relationship between LMP and coronary events in 12 months.
Methods: 109 cases of hospitalized patients with diabetes were divided into ACS group, stable angina pectoris (SAP) group and non-CHD group (P < 0.05). LMP had higher level in SAP group than non-CHD group (P < 0.05). 98 cases were of successful follow-up, lost in 11 cases. 24 cases of patients had cardiovascular events within 12 months, the LMP levels were significantly higher in patients with cardiovascular events than without cardiovascular events (P < 0.05). COX regression analysis showed that LMP was an independent risk factor for cardiovascular events in 12 months in patients with diabetes and ACS (P < 0.028).
Conclusion: The level of circulating LMP is an independent risk predictor of diabetic patients with ACS in recent cardiovascular events.

P1509 | BENCH
X-ray phase-contrast synchrotron radiation based micro-CT to study detailed cardiac anatomy, myofiber structure and vasculature of a rodent heart
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Purpose: Cardiac cell organization in a 3D fibre structure enables the heart to efficiently pump a large volume-fraction. Information on this complex organization is essential to understand diseases. Microscopy techniques provide sufficient detail, but 3D imaging of whole hearts often results in distortions of detailed geometry and fibres. CT/MRI resolution is usually too low to study cellular mechanics in detail. Therefore we developed a novel approach to study heart in great detail, but on the whole organ scale.
Methods: A young rat heart was formalin-fixed, ethanol-dehydrated and embedded in agarose. X-ray phase-contrast synchrotron radiation-based micro-CT was performed at 7.43 μm resolution (ESRF-ID19, 19keV). The heart was rotated over 360°. Five acquisitions were necessary to cover the whole heart along its long axis. The series were reconstructed using state-of-the-art filtered back-projection. The reconstructed volumes were merged into a single dataset covering the whole heart.
Results: Atria, ventricles, great vessels and valves can be clearly differentiated in a longitudinal reslicing of a dataset (Fig. 1A). Details of local complexity of the walls and part of the vasculature are visible (Fig. 1B, C). Using volume rendering, the detailed architecture of the ventricles can be observed in a transverse view (Fig. 1D). Fiber orientation can be recognised and the coronary vessels tree can be segmented.

Cardiovascular pathophysiology / Cardiac Pathophysiology
Conclusions: We have obtained novel, high-resolution, datasets of a whole heart providing structural information on microscopic level without the need of slicing. This opens up a new range of exciting possibilities for a systems approach towards cardiac structure and function, providing fast acquisition of the whole heart.

P1510 | BENCH
Neuregulin-1 preserves right ventricular diastolic function in animal model of pulmonary arterial hypertension
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Neuregulin (NRG)-1 is involved in the preservation of left ventricular performance. Nevertheless, the role of NRG-1 in pulmonary arterial hypertension (PAH) and right ventricular (RV) diastolic stiffness is unknown. We analysed the presence and possible underlying mechanisms of RV diastolic dysfunction in an animal model of PAH and the role of NRG-1 in this context.

Wistar rats randomly received monocrotaline (MCT, 60mg/Kg, sc) or vehicle. After 14 days, rats received NRG-1 (1mg/Kg, ip) or vehicle. The study resulted in 4 groups: control (CTRL, n=16); CTRL+NRG (n=15); MCT (n=13); MCT+NRG (n=18). RV invasive hemodynamic studies and sample collection were performed 25-28 days after MCT administration. Isolated cardiomyocytes were stretched to determine force generation and the phosphorylation of focal adhesions was analyzed (ProD Diamond and SYPRO Ruby protein gel stains). Only significant results (p<0.05) are given.

RV diastolic stiffness (β) was increased in MCT rats (MCT vs CTRL: 0.016±0.002 vs 0.008±0.001). However, NRG-1 treatment attenuated this change (MCT+NRG: 0.007±0.001). Histological analyses revealed increased cardiomyocyte cross-sectional areas (MCT vs CTRL: 536.67±59.46 vs 375.39±47.43μm2), indicating RV hypertrophy. In addition, the amount of RV fibrosis was enhanced in PAH tissue (MCT vs CTRL: 2.04±0.17 vs 0.98±0.57%). NRG-1 also attenuated both changes (MCT+NRG: 409.01±19.72μm2 and 1.00±0.17%, respectively). MCT-group isolated cardiomyocytes developed higher passive force when compared to CTRL-group cells at the sarcomere lengths of 2.0 μm (MCT vs CTRL: 1.90±0.43 vs 1.43±0.29N/m2), 2.2 μm (MCT vs CTRL: 3.66±0.69 vs 2.68±0.24N/m2), and 2.3μm (MCT vs CTRL: 5.76±1.15 vs 3.86±0.87N/m2). NRG-1 restored passive force development to levels similar to the CTRL-group, at 2.0, 2.2, and 2.3μm (MCT+NRG: 1.26±0.25, 3.04±0.55, and 4.75±0.99N/m2, respectively). CTRL-NRG treated cells developed less passive force compared to the CTRL-group (CTRL+NRG: 1.16±0.31, 2.27±0.38, and 3.05±0.54N/m2, at 2.0, 2.2, and 2.3μm respectively). Titin phosphorylation was reduced in RV tissue of MCT rats (MCT vs CTRL: 1.06±0.38 vs 1.62±0.85, arbitrary units) and increased in MCT+NRG group (2.28±0.61).

P1511 | BENCH
Vascular rarefaction mediates whitening of brown fat in obesity
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Brown adipose tissue (BAT) is abundant in newborn humans and small rodents. Recent studies have shown that human adults also possess active brown adipose tissue and it decreases with obesity and aging. In addition to its thermogenic function, it has been suggested that BAT contributes to systemic metabolism because of its high oxidative capacity. Several studies have demonstrated that vascularization in white adipose tissue is crucially involved in maintaining systemic metabolic homeostasis; however, the importance of vasculature in BAT is inadequately understood. In obesity, capillary rarefaction and mitochondrial dysfunction and loss in BAT can be associated with mitochondrial dysfunction and loss in adipocytes. The introduction of large lipid droplets and mitochondrial dysfunction and loss. These changes in the BAT microenvironment impair thermogenic responses and contribute to dysfunctions in glucose metabolism.

Diет induced obesity (DIO) model identified on a high fat high sucrose diet exhibited a marked increase in intra-cellular lipid droplet accumulation and a reduction in mitochondria number in brown adipocytes. DIO model displayed reduced adrenergic receptors and VEGF-A expression, capillary rarefaction and evidence of hyponxia. BAT whitening was also observed by the targeted ablation of Vegfa in adipose tissue of non-obese mice, which demonstrated an impaired systemic glucose metabolism and reduction in thermogenic response. The introduction of Vegfa specifically in obese mice reversed capillary rarefaction, ameliorated brown adipocyte dysfunction, and improved insulin sensitivity. An increase in ROS production and reduction in membrane potential were detected in mitochondria isolated from BAT of obese or Vegfa ablised mice, associated with a significant increase in autophagic responses. These changes were inhibited with the introduction of vegfa specifically into BAT. These data show that overnutrition promotes hyponxia in BAT, causing it to whiten through mitochondrial dysfunction and loss, subsequently contributing to impaired systemic glucose metabolism.

P1512 | BENCH
In vivo silencing of mitochondrial adapter p66Shc gene improves endothelial insulin resistance in obese mice
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Purpose: Insulin resistance is mostly driven by oxidative stress and inflammation. This condition precipitates type 2 diabetes and predicts long-term morbidity and mortality. However, the molecular link between obesity and impaired insulin signalling remains to be elucidated. Restoration of endothelial homeostasis has been recently shown to improve insulin delivery in other organs and prolong lifespan in mice. The mitochondrial adapter p66Shc is a key source of reactive oxygen species (ROS) in the endothelium. In this study we hypothesize that p66Shc-driven ROS production mediates endothelial insulin resistance in obesity.

Methods: Twelve obese lep-r mutant deficient mice (LepOb/Ob) and 12 wild-type littermates were used for all the experiments. In vivo gene silencing of p66Shc was performed by i.v. administration of a mix of 2 siRNAs specifically targeting p66Shc together with a cationic delivery reagent. Scrambled siRNA (sc.siRNA) was used as a control. Endothelium-dependent relaxation to insulin (10-6 to 10-3mol/L) was evaluated from femoral rings isolated from obese and lean mice. p66Shc expression was determined by immunoblotting and mitochondrial ROS measured by ESR spectroscopy. Furthermore, knockdown of p66Shc gene was performed by siRNA technology in endothelial cells (EC) isolated from LepOb/Ob and WT mice. Data are expressed as percentage of control.

Results: Obese mice showed an impairment of vasodilatatory response to insulin (27.8±2 vs 54.6%, p<0.01). Interestingly enough, p66Shc siRNA restored insulin-dependent relaxation as compared with sc.siRNA (40±6 vs 54.6±6%, p<0.01), mimicking the effect of insulin silencing in adipocytes. Treatment of obese mice was explained by suppression of inhibitory Ser-636 phosphorylation of insulin receptor substrate-1 (IRS-1) and restoration of Akt/Enos pathway. In endothelial cells isolated from LepOb/Ob mice p66Shc silencing significantly blunted ROS generation. This finding was associated with improved insulin-dependent activation of Akt and Enos. Treatment of obese mice was explained by suppression of inhibitory Ser-636 phosphorylation of insulin receptor substrate-1 (IRS-1) and restoration of Akt/Enos pathway. In endothelial cells isolated from LepOb/Ob mice p66Shc silencing significantly blunted ROS generation. This finding was associated with improved insulin-dependent activation of Akt and Enos.

Conclusion: p66Shc-driven oxidative stress is an important determinant of endothelial insulin resistance in obese mice. Targeting p66Shc may represent a promising strategy to improve NO availability and insulin signalling and, hence, prevent adverse cardiometabolic effects in obese patients.

P1513 | BENCH
Aerobic training regulate cardiac miRNA-208a and MED13 levels preventing obesity in Zucker rats
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Aerobic exercise training (ET) has been established as an important treatment for obesity, however, underlying mechanisms remain to be further determined. MicroRNAs (miRNAs) inhibit protein expression by base-pairing with the 3’ UTRs of mRNA targets. MiRNA-208a is a cardiac-specific miRNA that regulates β-MHC content and systemic energy homeostasis via MED13, a subunit of the Mediator complex. We investigated whether ET regulates the miRNA-208a and their target MED13 expression in brown adipose tissue (BAT) and the effects on BAT-related with the weight loss in obese Zucker rats (OZR). OZR (n=10) and Lean (L, n=10) male rats were assigned into 4 groups: OZR, trained OZR (OZRT), L and trained L (LT). Swimming ET consisted of 60 min of duration, 1/day/10 weeks, with 4% caloric body weight workload. OZRT groups showed a significant augment in the body weight compared with L group. However, ET was effective in reducing weight gain in OZRT (59%) compared with OZRT group. In accordance, ET reduced 20% visceral fat weight in OZRT compared with OZRT group. Cardiac miRNA-208a expression was analyzed by real-time PCR increased 57% in OZRT paralleled with a decrease of 39% in MED13 protein levels analyzed by western blot compared with L group. In contrast, ET corrected the cardiac miRNA-208a and MED13 levels in OZRT compared with L. Furthermore, ET reduced the increased cardiac mass (13%), normalized β-MHC mRNA and protein levels and improved the loss of diastolic function caused by obesity. These results suggest that ET can prevent weight gain via increased of cardiac MED13 and pathological cardiac hypertrophy via β-MHC reduction by regulation of miRNA-208a, indicating the heart in the systemic metabolic control and the miRNA-208a as potential therapeutic target for metabolic and cardiac disorders.
P1515 | BENCH
Mechanisms of increased oxygen radical formation in alcoholic cardiomyopathy in a mouse model of acetaldehyde overload and potential therapeutic approaches
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Background: Growing evidence suggests, that NADPH-oxidases (NOX) are involved in the pathogenesis of ethanol related organ damage. We sought to investigate the role of NADPH oxidase derived superoxide in the development of alcoholic cardiomyopathy (ACM) using ALDH-2−/− mice as an animal model of acetaldehyde overload and whether pharmacologic or genetic ablation of NOX2 could beneficially influence the disease model.

Methods: Male B6, ALDH2−/− and ALDH2−/−NOX2/g91phox−/− were fed a 2% ethanol vs. liquid control diet. Iter 5 weeks, cardiac function was assessed with echocardiography, malondialdehyde levels in internal organs were measured by dot blot. NOX activity in cardiac membrane fractions was quantified by chemiluminescence, while the expression of NOX2 was assessed by WB. For in vitro studies, cardiomyocytes (CMs) were isolated from B6 mice via cannulation and retrograde perfusion of the aorta. Plated CMs were incubated in culture media containing increasing concentrations of ethanol (EtOH) or acetaldehyde (MeCHO) in the presence or absence of the NOX inhibitor apocynin. Subsequently, CM mitochondrial membrane potential and mitochondrial ROS production was assessed by automated cellular imaging using the fluorescent probes TMRM+ and MitoSOX. Results: ALDH2−/− fed the 2% ethanol diet displayed a significantly decreased LV systolic function compared to ALDH2−/− fed the liquid control diet and to B6 mice. Furthermore, ethanol-fed ALDH2−/− mice exhibited significantly increased levels of malondialdehyde in internal organs (highest in the heart), increased heart/body and lung/body weight ratios, significantly increased cardiac NOX activity and significantly increased expression of the NOX2 subunit p67phox and the NOX2 activator Rac1 compared to control fed ALDH2−/− and B6 mice. These results were corroborated by in vitro studies: cultured CMs which incubated with media containing MeCHO showed significantly increased levels of mitochondrial ROS and significantly decreased mitochondrial membrane potential. Pharmacologic ablation of NOX in CMs exposed to MeCHO lowered mitochondrial ROS and partially preserved mitochondrial membrane potential. Finally, we subjected mice double negative for ALDH2 and NOX2/g91phox to the ethanol diet for 5 weeks. Echo revealed that the additional lack of NOX2/g91phox protects mice from the acetaldehyde-overload induced cardiomyopathy.

Conclusions: In vitro and in vivo results show that NOX derived ROS contribute to the development of ACM. We further provide evidence that ablation of NOX-2 can beneficially influence the disease in in vitro and in vivo.

P1516 | BENCH
Nav1.5 N-terminus is responsible for the Nav1.5 and Kir2.x reciprocal modulation
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Purpose: It has been demonstrated that the N-terminal domain of Nav1.5 channels (Nav1.5 N-terminus) is involved in the modulation of Kir2.x channels. However, the complete mechanism of the reciprocal modulation of Kir2.x channels by the Nav1.5 N-terminus remains to be elucidated. This study aimed to investigate the mechanism of the reciprocal modulation of Kir2.x channels by the Nav1.5 N-terminus.

Methods: Kir2.1, Kir2.2, Kir2.3 and Kir2.4 channels were heterologously expressed in HEK293 cells in the presence or absence of the NOX inhibitor apocynin. Subsequently, CM mitochondrial membrane potential and mitochondrial ROS production was assessed by automated cellular imaging using the fluorescent probes TMRM+ and MitoSOX. Results: Cotransfection of Nter with Kir2.1 and Kir2.2 channels significantly increased Kir2.1 current (Kir2.1) and Kir2.2 measured at -126 mV from -126 ± 12 to -183 ± 18 pA/pF (n=25, P<0.05) and from -72 ± 9 to -114 ± 13 pA/pF (n=22, P<0.05), respectively. Conversely, cotransfection of Nter with Kir2.3 channels, which did not bind to syntrophin with a high affinity as demonstrated in immunoprecipitation experiments, did not significantly modify Kir2.3. Nter did not increase the current density generated by Nav1.5 channels lacking their C-terminal PDZ domain (Nav1.5.PDZ). Noteworthy, Nav1.5.PDZ channels still co-immunoprecipitated with syntrophin. We identified in the Nter peptide a sequence which could act as a “PDZ-like” binding domain (18-RESLA) and we tested its involvement in the Nter “chaperon” effect by site directed mutagenesis. The results demonstrated that mutants of all residues, except p.S20A, Nter, increased Kir2.2. To further confirm the role of Ser20, p.S20A Nav1.5 channels were cotransfected with either Kir2.1 and Kir2.2 channels. Cotransfection of Kir2.1 channels with p.S20A Nav1.5 channels did not increase Kir2.1 as cotransfection with Nav1.5 channels did (from -126 ± 12 to -192 ± 16 pA/pF, n=35, p<0.05). Finally, to test the Nav1.5 chaperon effect in a cardiac model, adult rat ventricular myocytes were enzymatically dissociated, cultured, and infected with either a control adenoviral construct (Ad-GFP) or an Nter cDNA adenoviral construct (Ad-Nter). Results: demonstrated that myocyte infection with Ad-Nter significantly increased both the inward sodium (INa) and inward rectifier (IK1) currents.

Conclusions: The N-terminal domain of Nav1.5 channels exerts “chaperon-like” effect on Kir2.x channels. This effect depends on the residue Ser20, which probably determines the binding of syntrophin via an “internal” PDZ binding domain.

P1515 | BENCH
Characteristics of pre-clinical models for the study of atherosclerosis and restenosis
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Purpose: Animal models are necessary for the evaluation of new endovascular therapies. We compared relevant models of restenosis with and without atherosclerotic injury in pigs and rabbits. Our aim was to compare the characteristics and feasibility of these models.

Methods: We compared atherosclerotic lesions induced by balloon injury and atherogenic diet in pig coronary arteries (n=33) and rabbit aorta (n=12). We also studied the lesions of WHHL rabbits (n=6), which portray a familiar hypercholesterolemia type phenotype and have naturally high circulating cholesterol levels. In-stent restenosis (ISR) was also evaluated in different branches of the pig coronary tree by OCT imaging (n=17). Stents were implanted in the right (RCA), the left anterior descending (LAD) and left circumflex (LCX) coronary artery.

Results: Injured rabbit aortas developed lipid rich and uniform lesions. Porcine coronary injury produced lesions with varying characteristics and creation of lipid rich lesions was difficult even with high fat diet (picture). OCT follow up revealed very different characteristics in the different coronary branches in regards to the formation of in-stent restenosis. The RCA was found most resistant to ISR (RCA 17.9±3.5% vs LAD 33.7±3.8% vs LCX 39.9±9.2%) six weeks after stent implantation.

Conclusions: The rabbit aorta with double injury of high cholesterol and mechanical de-endothelialization produced most atherosclerosis-like lesions. The
P1518 | BENCH
ATP mediated signaling in pre-sympathetic area of the brainstem is critical for development of hypertension in spontaneously hypertensive rats
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Purpose: Increased sympathetic tone is associated with the development and progression of essential hypertension. Pharmacological studies have shown a direct stimulatory effect of ATP on bulbospinal pre-sympathetic neurons, resulting in increased sympathetic tone and BP. Here, we explored whether reduction of extracellular ATP in the rostroventral lateral medulla oblongata (RVLM), a brainstem region containing sympathoexcitatory pre-sympathetic neurons, affects development of hypertension in spontaneously hypertensive rats (SHRs).

Methods: We developed a lentiviral vector (LVV) to drive the expression of a potent membrane-bound ectonucleotidase – transmembrane pyrophosphatase (TMP AP) for facilitated breakdown of extracellular ATP. LVV-TMPAP or control LVV-GFP were injected stereotaxically into the RVLM of pre-hypertensive (8-weeks-old) spontaneously hypertensive rats (SHRs) and age-matched Wistar rats. Blood pressure measurements were performed by occlusive tail cuff method. Measurements were commenced 1 week after the injections and repeated weekly for 8 weeks. Data is expressed as mean ± SEM and one-way ANOVA was used to assess statistical significance.

Results: Expression of TMPAP in the RVLM of SHRs resulted in a significant reduction in arterial blood pressure. Three weeks after the injections, SHRs transduced to express TMPAP in the RVLM had mean arterial blood pressure of 115.6±8.8 mmHg (n=7), which was significantly (p<0.009) lower than that in SHRs transduced to express GFP (152.9±8.4 mmHg, n=9). In comparison, TMPAP expression in the RVLM had no significant effect on the mean arterial blood pressure of control rats (91.4±4.5 vs 92.6±3.5 mmHg, p=0.836, n=8 in both groups).

Conclusions: Increased breakdown of extracellular ATP in the sympathoexcitatory circuits of the brainstem attenuated the development of hypertension in SHRs. ATP mediated signaling in the pre-sympathetic area of the brainstem appears to be critical in the development of essential hypertension.

P1521 | BENCH
Mediators of oxidative stress in atrial myocardium in Zucker Diabetic Fatty rats
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Purpose: Hyperglycemia induces the production of reactive oxygen species in cardiac myocytes. Cell death by apoptosis is the predominant damaging mechanism in diabetic cardiomyopathy. Cardiacocyte death causes loss of contractile tissue and initiates cardiac remodelling processes. The mediators of oxidative stress and apoptosis in atrial myocardium in the presence of diabetes type 2 are not described so far.

Methods: Zucker Diabetic Fatty (ZDF) rat is an animal model that mimics human diabetes mellitus type 2 (T2DM). Left and right atrial tissue samples from male rats (obese ZDF; n=8) and their non-diabetic controls, lean ZDF (n=6), were analysed at the age of 12 weeks (onset of diabetes) and 24 weeks (advanced stage). Atrial tissues were analysed at the transcriptional and protein levels. Analyses focused on the expression of indicative markers of oxidative stress, NADPH oxidases, LOX-1, and the apoptosis markers, bax, μ-calpain, and caspase 3, during the progression of T2DM severity. Moreover, the possible contribution of MAPK activation to pro-apoptotic pathways of myocardial hypertrophy was also studied.

Results: The atrial tissue expresses three isoforms of catalytic subunits of NADPH oxidase: NOX1, NOX2 and NOX4. T2DM leads to an increased expression of NOX1, and NOX2 in atrial tissue. Interestingly, the expression of NOX4 increased at the transcriptional level only. Transcriptional reduction of the α1 subunit of LOX-1 was detected at the mRNA level. The protein level of the α1 subunit of LOX-1 was elevated at the onset of diabetes only. Increased oxidative stress facilitates the oxidation of low density lipoproteins (LDL). As a consequence, the expression of the receptor for oxidized LDL remained continuously increased at the transcriptional (2.2±0.36;p=0.01) and protein level (2.0±0.19; p=0.01) atrial tissue of diabetic hypertrophic cardiomyocytes. The finding confirmed the results of binding competition assays. Additional, T2DM-dependent oxidative stress activates pro-apoptotic mechanisms in atrial tissue. With disease progression we could detect enhanced expression of μ-calpain (mRNA 1.8±0.20; protein 2.0±0.34; p<0.05), an enzyme responsible for disintegration of sarcomeric structure and initiation of apoptosis. Immunoblot analysis also showed the occurrence of active caspase 3 in atrial tissue of diabetic rats at the age of 6 months. Immunoblot analyses further revealed that the “oxidative state” in atrial tissue is not accompanied by either activation of MAP kinases, or by activation of the canonical NF-κB.

Conclusions: Our data show that T2DM is associated with significantly altered atrial expression of NADPH oxidase and LOX-1. The persistence of oxidative stress in atrial tissue facilitates apoptosis and induces calpain responsible for degradation of myofilobulbary proteins.

Carcinogenesis / Cardiovascular disease

P1520 | BENCH
Role of FGF21 in the control of UCP3 in the heart
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Introduction: Uncoupling protein 3 (UCP3) is a member of the mitochondrial anion carrier superfamily of proteins uncoupling mitochondrial respiration. It has been shown that UCP3 is expressed in the heart and it has been involved in the protection against heart failure by prevention of reactive oxygen species (ROS) production. We have recently shown that FGF21, an endocrine member of the FGF family, is produced by the heart and exerts protective effects preventing cardiac hypertrophy development. The aim of the study was to determine the role of FGF21 on UCP3 expression in the heart.

Methods: Studies in vivo were performed in hearts from wild-type (wt) and Fgf21-null mice. To assess the effects of the inflammatory process, mice were subjected to intraperitoneal (i.p.) injection of lipopolysaccharide (LPS) for 4 hr. To induce cardiac hypertrophy mice were subjected to isoprotenerol (ISO) infusion for 7 days. Cell culture of neonatal cardiomyocytes from rats and raven were used for the in vitro studies. Cardiomyocytes in culture were treated with LPS for 24 hr in the presence or absence of FGF21.

Results: We found that treatment of FGF21 in cardiomyocytes in culture induces the expression of UCP3. Moreover, FGF21 reduces reactive oxygen species production in cardiac cells. In keeping with this, Fgf21-null mice presented reduced expression of UCP3 in response to stimulation with LPS-induced pro-inflammatory pathways or ISO-induced cardiac hypertrophy in the heart. Moreover, we showed that FGF21 is expressed in and released by cardiomyocytes in response to LPS, and its expression is under the control of the Sirt1 (sirtuin-1) pathway. Using neonatal cardiomyocytes in culture from wt and Fgf21-null mice we found that the FGF21 released by cardiomyocytes acts in an autocrine manner to protect the cells against oxidative stress.

Conclusions: Our data indicate that FGF21 regulates in an endocrine/autocrine manner UCP3 expression thus preventing reactive oxygen species production in cardiac cells. Therefore FGF21 acts in the heart as an antioxidant factor preventing pro-oxidative pathways induced by inflammatory/hypertrophic conditions.
we showed that the dysregulation of P1O1 occurs at the level of its P-subunits in pAF patients, which may explain the subcellular heterogeneity in P1O1 activity and downstream protein phosphotyrosine observed in AF. This represents a novel concept in AF pathogenesis and may provide more specific drug targets for treating AF.

P1523 | BENCH
Moderate PGC-1alpha1 expression in the heart induces unique functional phenotype without metabolic remodelling
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Peroxisome proliferator-activated receptor gamma co-activator alpha (PGC-1α) is a master regulator of cardiac metabolism activating signalling cascades through PPARα and ERRβ. It has been shown that robust, cardiac specific over expression of PGC-1α leads to metabolic remodelling with subsequent functional complications. However, the role of moderate PGC-1α expression associated with physiological adaptations, like the one resulting from endurance training increasing the expression by 2-4-fold, is yet to be clarified. To elucidate this we have studied the phenotype of a mouse model in which PGC-1α transgene is driven by muscle creatine kinase (MCK) promoting only modest (3-4-fold) cardiac over expression of PGC-1α. Importantly, we found that aspects of cardiomyocyte electrophysiology of transgenic hearts and done in vitro analysis of metabolism. The findings from our in vivo experiments propose, that PGC-1α, in Tg mice have a clear dilatation of the left ventricle without heart failure, whereas in vitro studies showed no metabolic remodelling or altered mitochondrial density of cardiomyocytes but increased Ca2+ sensitivity of the contractile element and decreased expression of ryanodine receptor 2. Collectively, our data suggests that PGC-1α has unknown targets, different from those mediated by PPARα and ERRβ that shape the functional phenotype of cardiomyocytes without interfering with metabolism.

P1524 | BEDSIDE
Insulin resistance is associated with cardiac aging and shorter leukocyte telomere length

Purpose: Cardiac aging is an independent risk factor for cardiovascular disease. The main signs of the aged heart are a thickening of the left (LV) ventricular walls and LV diastolic dysfunction. Insulin resistance (IR) is exacerbating aging-related changes in the cardiac structure and function. One possible mechanism underlying IR-induced cardiac dysfunction with advancing age could be related to decreased telomere length of leukocytes (LTL). Telomeres are tandem repeats of the DNA sequence at the end of chromosomes and protect DNA molecule from damage. LTL is a marker of replicative aging. Our hypothesis is that IR led to shorter telomeres and senescent phenotypes in the heart.

Methods: We investigated 118 non-obese participants aged 60 to 85 years without history of CVD, diabetes and regular drug medication. All the volunteers underwent standardized transesophageal echocardiography with the available system (iE33, Philips), had an oral glucose tolerance test. HOMA-IR was calculated as fasting insulin (mU/ml) x fasting glucose (mmol/l) /22.5. IR was diagnosed in case of HOMA-IR elevation >2.5 based on reference. LTL was measured by real-time quantitative polymerase chain reaction. We determined the relative ratio of telomere repeat copy number (T) to single-copy gene copy number (S).

Results: In older individuals HOMA-IR was significantly positively related to LV septal wall thickness (r=0.49, p<0.001), LV posterior wall thickness (r=0.458, p<0.001), E/Em (r=0.379, p<0.01) and inversely correlated with E/A (r=-0.320, p<0.01). LTL was significantly and independently associated with age (β=-0.026, p=0.015) and HOMA-IR (β=-0.176, p=0.027). Results of analysis of variance (ANOVA) showed that LTL was significantly correlated to diastolic function indices regardless of age (p<0.001). Older subjects with higher HOMA-IR had a shorter telomeres (p=0.046) and more expressed LV hypertrophy and diastolic dysfunction to compared to subjects with normal HOMA-IR. Individuals with IR did not significantly differ from those with normal HOMA-IR in the proportion of smokers, or levels of blood pressure and BMI.

Conclusions: These findings suggest that insulin resistance is associated with more expressed signs of the aging heart and shorter LTL. Accelerated telomere attrition appears to be the mechanism by which impaired insulin resistance develops into cardiac aging.

P1525 | BENCH
From beat rate variability in induced pluripotent stem cell-derived pacemaker cells to heart rate variability in human subjects
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Numerous studies showed that heart rate (HR) fluctuates around a mean, a phenomenon termed HR variability (HRV). A key feature of human SAN is that HRV exhibits high similarity contributing to its complexity. We hypothesized that human embryonic stem cell-derived cardiomyocytes (CM) and iPSC derived CM (IPSC-CM) exhibit beat rate variability (BRV), fractality and power-law behavior resembling HRV in human SAN. To investigate whether cellular BRV is a source of HRV, we hypothesized three-levels of interaction among different cardiomyocyte entities: (1) single pacemaker cells, (2) networks of electrically coupled pacemaker cells, (3) in situ SAN. To test this hypothesis, we analyzed HRV properties in ECGs of healthy volunteers, and BRV in extracellular electrogagrams and action potentials of spontaneously contracting embryoid bodies (EBs) and iPSC-CM, respectively, both fabricated from volunteers’ keratinocytes. We also hypothesized that disrupting intracellular Ca2+-handling impacts on BRV. The major findings were: (1) Marked BRV/HRV were present at all three levels, reflected by Standard Deviations (STD) of inter-beat intervals (IBIs) and Poincare plot SD1 and SD2. (2) BRV indices were greater in single cardiomyocytes than in networks or heart, suggesting the large increase in BRV occurs in transitioning from net-work to single cardiomyocyte. We also compared BRV among single cells, small (~5–10 cells) and larger EBs (~10 cells); BRV indices progressively increased as cells were formed into networks. These findings illustrate that as more cells are included in the network, BRV decreases sharply, suggesting the higher the number of interactions among the potential pacemakers, the smaller the variability around the mean beat rate. Further, we found that BRV magnitude is similar within the group including the heart, EB and the large cluster, but are significantly (P<0.05) larger upon transitioning to the small cluster and a single cell. Finally, disrupting intracellular Ca2+-handling by means of RU360 (mitochondrial Ca2+ -uptake blocker), GCP-37157 (mitochondrial Na+-Ca2+ exchanger antagonist) and ryanodine, markedly decreased BRV magnitude, suggesting that intracellular mechanisms contribute to BRV/HRV and the fractal behavior of heart rhythm. The decreased BRV magnitude in transitioning from single cell to EB suggests that HRV of hearts in situ originates from summation and integration of multiple cell-based oscillators. Hence, we hypothesize interactions among multiple pacemaker cells and intracellular Ca2+-handling mechanisms determine HRV in humans and isolated cardiomyocyte networks.

P1526 | BENCH
Morphometric characterization of intracardiac neurons modulating atrial electrophysiology
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Purpose: Neuronal modulation is a key element in the regulation of heart rate and rhythm. As has been demonstrated by anatomical studies, intrinsic cardiac neurons (ICN) on the level of the atria form a complex network. Although it is well known that ICN are involved in the pathophysiology of atrial fibrillation, detailed morphometric and functional characterization of these cells has not yet been undertaken.

Methods: Hearts were harvested from the hearts of male mice, aged between 12 and 16 weeks (C57BL/6, Charles River, France). Epicardial fat at the dorsal surface of the atria and in between the great vessels, containing the bulk of ICN, were removed from the hearts of mice. The remaining atrial tissue was dissected, incubated for 48h (37°C, 5% CO2) ICN were digitally photographed and assessed upon transiting to the small cluster and a single cell. Finally, disrupting intracellular Ca2+- handling means of RU360 (mitochondrial Ca2+ -uptake blocker), GCP-37157 (mitochondrial Na+-Ca2+ exchanger antagonist) and ryanodine, markedly decreased BRV magnitude, suggesting that intracellular mechanisms contribute to BRV/HRV and the fractal behavior of heart rhythm. The decreased BRV magnitude in transitioning from single cell to EB suggests that HRV of hearts in situ originates from summation and integration of multiple cell-based oscillators. Hence, we hypothesize interactions among multiple pacemaker cells and intracellular Ca2+-handling mechanisms determine HRV in humans and isolated cardiomyocyte networks.

Results: Under adapted culture conditions ICN, as well as atrial myocytes remained viable for extended periods (7-72h), with myocytes exhibiting habitual proliferation and spontaneous contractility, while ICN showed axonal outgrowth. These relations of neuronal cultures could be demonstrated in distinct distribution: 1) unipolar ICN (27.0%), 2) bipolar ICN (42.3%), 3) multipo- lar ICN (30.8%). Following the loss of axons during the isolation process, ICN exhibited characteristic axonal outgrowth according to their cell type, with unipo-
lar (90.7±10.3μm) and bipolar (73.4±10.6μm) showing typically longer axons, than the smaller multipolar ICN (35.7±5.6μm; p=0.0013). In the FACS analysis ICN could be identified as a discrete population positive for TH, ChAT and NFL.

**Conclusions:** Our findings demonstrate the feasibility of isolation and cultivation of adult murine ICN, exhibiting characteristic distribution of cell types and rate of axonal outgrowth. Furthermore ICN can be kept in stable co-culture with atrial myocytes. These methods enable detailed in-vitro studies looking into the complex interaction of atrial neurons and myocytes, one key mechanism in the pathophysiology of atrial fibrillation.

**P1527 | BEDSIDE**

Different profile of serum miRNA in patients with patent vs. occluded target vessel in acute coronary syndrome

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Circulating microRNAs (miRs) are recognized as useful cardiovascular biomarkers in acute coronary syndromes (ACS). Vessel occlusion is not always manifested with ST-elevation; no specific biomarkers have been identified to differentiate between patent or occluded infarct-related coronary artery (IRA), so far. However, data indicate possibility of IRA occlusion in the absence of ST-elevation which unfortunately leads to delays in diagnosis and revascularisation therapy.

**Methods:** Forty-four consecutive patients (mean age 57±5.9 years) with unobstructed patent or positive troponins were admitted. Patients were classified into 2 categories, with respect to patent vs. occluded IRA and those with ST-elevation or non-ST-elevation MI (STEMI vs. NSTEMI). On admission, inflammatory markers (hs-CRP, fibrinogen, TNF-α and IL-6) and expression levels of selected serum cardiac and brain-ischemia induced miRNAs (miR-1, -16, -34a, -122, -124, -208b, -133a/b, -375, and -499) were analyzed.

**Results:** There were 17 STEMI and 27 NSTEMI. Of those, occluded IRA was found in 15 NSTEMI subjects and 13 STEMI patients, while the remaining subjects from STEMI and NSTEMI group had a patent IRA during coronary angiography. Summarizing, 16 patients were categorized to the patent and 28 to the occluded groups; consistently, STEMI vs. NSTEMI patients had significantly higher troponin T levels, lower fibrinogen concentration (3.4±1.2 vs. 4.4±1.78g/L; p=0.049), and a 3.83-fold higher miR-134 expression (p<0.05). Whereas, patients with the occluded vs. patent IRA had significantly higher levels of circulating miR-133a (fold change: 7.00), miR-133b (4.57), miR-34a (5.50), miR-124 (2.55) and miR-134 (3.45), but no difference in the levels of troponin T and inflammatory markers. ROC analysis showed that predictors of IRA occlusion are: expressions of miR-124 (area under the curve; AUC: 0.787, sensitivity of 78%, specificity of 63%, p=0.002), miR-133b (AUC: 0.704; sensitivity of 63%, specificity of 74%, p=0.027) and miR-134 (AUC: 0.686; sensitivity of 69%, specificity of 60%, p=0.043). With respect to STEMI vs. NSTEMI group, only miR-134 showed differential expression (p=0.015); sensitivity of 63%, specificity of 60% (p=0.015).

**Conclusions:** miR expression do not discriminate patients with STEMI and NSTEMI, with the only exception to miR-134. Suprisingly, higher expression levels of several cardiac and brain miRs were related to IRA occlusion. Discriminating value of miR-133b and miR-134 in indicating patients with IRA occlusion, thus requiring urgent coronary revascularisation, despite the lack of ST-elevation on ECG needs to be established.

**P1528 | BENCH**

Oral pretreatment with a green tea polyphenol ameliorated renal impairment in a cardiopulmonary bypass model for diabetic rats

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**Purpose:** Acute kidney injury (AKI) is a common and serious postoperative complication following exposure to cardiopulmonary bypass (CPB), and diabetes mellitus is an independent risk factor for AKI after cardiac surgery. Epigallocatechin-3-gallate (EGCG), a major polyphenolic component of green tea that we reported its cardiovascular properties previously, is thought to have a renoprotective effect through its diverse biochemical activities. We investigated the effects of EGCG on renal damage in a CPB model for diabetic rats.

**Methods:** The Goto-Kakizaki (GK) rats, non-obese Wister substrains which develop type 2 diabetes mellitus early in life (300-360 g), were randomly assigned to 1 of 3 groups: Sham (n=10), CPB (CPB alone, n=9), or EGCG (CPB+EGCG, n=7). The EGCG group was given EGCG solution orally at 1 mmol/L for 2 weeks; the Sham and CPB groups received tap water alone for 2 weeks. Subsequently, CPB was performed for 30 min at a flow rate of 100 ml/kg/min in the CPB and EGCG groups. 24 hours after CPB, we compared renal function markers and histologic changes.

**Results:** Compared with the CPB group, the EGCG group exhibited limited histological tubular injury (P=0.04), and reduced gene expression of kidney injury molecule-1, a biomarker for renal tubular injury (Kid-1; P=0.021) and hemoxygenase-1, an ubiquitous enzyme up-regulated in response to oxidative stress and inflammatory stimuli (HO-1; P=0.022) (Fig. 1). There was no significant difference in the level of serum tumor necrosis factor-alpha between the CPB and EGCG groups.

**Conclusions:** These findings suggest that oral pretreatment with EGCG alleviates the kidney damage in a CPB model for diabetes rats by its antioxidative properties.

**P1529 | BENCH**

Macroscopic, microscopic and molecular characterization of myocardial fibrosis in a swine model of reperfused myocardial infarction


**Purpose:** Fibrosis plays a key role in the pathophysiology of left ventricular (LV) remodelling after myocardial infarction (MI). The dynamics of this process and whether it is a localized or diffuse phenomenon has not been totally clarified. We aimed to characterize these issues in a swine model of reperfused anterior MI.

**Methods:** Swine were subjected by means of percutaneous balloon inflation to a transient 90-min occlusion of mid left anterior descending artery followed by 72-h (acute MI model) or 1-month (chronic MI model) reperfusion. The extent of fibrosis was macroscopically (triphenyltetrazolium staining, % of LV volume) and microscopically (Sirius red staining, % of field) quantified in the infarct, adjacent and remote areas as well as in controls. TGF-β1, collagen-A1, A2 and A3 gene expression was determined.

**Results:** Macroscopically, necrosis (16±5% in the acute MI model) and fibrosis (16±4% in the chronic MI model) were detected in all cases. Macroscopic fibrosis occurred in the infarct but not in the adjacent or remote areas (figure). At microscopic level, in comparison with controls, fibrosis was only significantly increased in the chronic MI model at the infarct area (35±4%; p=0.001) but not in the acute MI model or in the adjacent and remote areas in the chronic MI model (~4% in all cases, p=ns, Figure). TGF-β1 (p=0.05, acute and chronic MI models, figure) and collagen-A1, A2 and A3 (p=0.001, chronic MI model) gene expression was significantly increased in the infarct but not in the adjacent or remote areas (p=ns).

**Conclusion:** In a model of anterior MI, 1-month after reperfusion, at macroscopic, microscopic and molecular levels, myocardial fibrosis appears as a localized process which mainly affects the infarct area but not the adjacent or remote regions.

**EXPLORING ATRIAL FUNCTION BY ECHOCARDIOGRAPHY**

**P1531 | SPOTLIGHT**

Left atrial strain as independent parameter to predict left ventricular diastolic pressure

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**Background:** Several invasive measurements are widely applied to estimate left ventricular filling pressures (LVFP) and to establish a correct therapeutic strat-
In a lot of cardiac diseases, especially in patients with heart failure. Among these, left atrial (LA) deformation analysis by speckle tracking echocardiography (STE), has recently demonstrated to be highly accurate to estimate LVFP even in patients with advanced heart failure. The aim of this study was to examine the accuracy of LA strain in predicting LVFP, analyzing its dependency from left ventricular parameters.

Methods: A total of 87 stable patients with sinus rhythm undergoing cardiac catheterization were studied. LV end diastolic pressure (LVEDP) was obtained during cardiac catheterization; peak atrial longitudinal strain (PALS), mean E/E' ratio, left ventricular longitudinal strain (GLS) and mitral annular plane systolic excursion (MAPSE) were measured in all subjects by another independent operator. PALS values were obtained by averaging all segments (global PALS), and by separately averaging segments measured in the 4-chamber and 2-chamber views.

Results: Global PALS correlated significantly with LVEDP (r=0.86; p<0.0001). Lower levels of correlation were found for E/E' ratio (r=0.57; p=0.01), GLS (r=0.40; p=0.05) and MAPSE (r=-0.22; p=ns). Parameters of LV systolic analysis presented lower correlation in subgroup of patients with lower LV ejection fraction. ROC analysis showed global PALS as the best predictor of increased LVEDP (AUC: 0.83). In multivariate analysis, global PALS emerged as a determinant of the LVEDP, independently on other confounding factors.

Conclusions: In comparison to E/E' ratio and LV systolic parameters, LA strain is a strong and independent parameter for non invasive prediction of LVEDP.

P1532 | BEDSIDE
Diagnosing paroxysmal atrial fibrillation in patients with ischemic strokes and transient ischemic attacks using echocardiographic measures of left atrium function
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Background: The underlying cause of ischemic strokes (IS) and transient ischemic attacks (TIA) is not identified in 25% of the cases. However, asymptomatic paroxysmal atrial fibrillation (P-AF) is often suspected to be the cause of the cryptogenic IS or TIA. Therefore, the aim of this study was to examine if echocardiographic measures of left atrial (LA) function including LA emptying fraction (LA EF) and minimal LA volume (min LAV) could diagnose PAF in patients with IS and TIA.

Methods: We retrospectively included 219 patients who after acute IS or TIA underwent a transthoracic echocardiographic examination in sinus rhythm. Patients were designated as PAF-patients if they had one or more reported incidents of AF before or after their echocardiographic examination.

Results: Patients in the PAF group were significantly older (61±13 vs. 51±14 years, p<0.001) than patients without PAF. Besides age, no other baseline characteristic (sex, hypertension, diabetes, cholesterol) was associated with PAF. None of the conventional echocardiographic parameters (LV ejection fraction, LV volumes, E/A-ratio, deceleration time, maximal LAV) were significantly associated with PAF. However, the atrial measures evaluating LA function (min LA volume and the LA EF) were significantly different (LA EF: 45±10% vs. 50±10%, p=0.041; min LAV: 30.2±17.3 mL vs. 24.3±9.8 mL, p=0.001) in patients with PAF, even after adjusting for age and gender (p<0.05 for both). Using joint criteria for LA dysfunction (above the cut-off values of age, LA EF and min LAV (with highest sensitivity and specificity determined from the ROC-curves), the diagnostic accuracy of PAF improved, resulting in a sensitivity of 95% and negative predictive value of 97% (See Table).

Diagnostic accuracy for age/LAEF/min LAV

Sensitivity Specificity PPV NPV
Age ≥60 years 63.64% 70.86% 35.44% 88.57%
Age ≥60 years and LA EF < 45% and/or min LAV > 23 mL 95.45% 32.57% 26.25% 96.61%
LAEF: left atrium emptying fraction; min LAV: minimum left atrium volume, PPV: positive predictive value; NPV: negative predictive value.

Conclusion: In patients with IS and TIA, measures of LA function (min LAV and LA EF) are independently associated with the presence of PAF. Applying these may yield better risk stratification for PAF-patience in patients suffering cryptogenic IS and TIA.

P1533 | BEDSIDE
Total atrial conduction time evaluated with tissue Doppler imaging predicts cardiac prognosis in patients with chronic heart failure
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Purpose: It has been proposed that total atrial conduction time is a marker of atrial remodeling, a novel echocardiographic parameter based on tissue Doppler imaging (TDI) has been used to assess the total atrial conduction time. The aim of this study was to investigate whether total atrial conduction time predicts poor prognosis in patients with chronic heart failure (CHF).

Method: Transthoracic echocardiography was performed at discharge in 42 consecutive CHF patients with sinus rhythm (26 males, mean age 67±14 years) who were hospitalized for heart failure. Total atrial conduction time was estimated by measuring the time delay between the onset of the P-wave of electrocardiogram and the peak A’-wave on the TDI of the left atrial lateral wall (PA-TDI duration).

Results: There were 11 cardiac events (26%) during a median follow-up period of 311 days. There were no significant differences in left ventricular end-diastolic dimension and ejection fraction between patients with and without cardiac events. Patients with cardiac events were significantly older and had larger left atrial (LA) dimension and longer PA-TDI duration (144 vs. 123 ms, P<0.01) than those without events. Multivariate Cox proportional hazard analysis showed that PA-TDI duration was an independent predictor for cardiac events (hazard ratio 4.113 (per 1 SD increase), 95% confidence interval 1.320-22.740, P=0.05). ROC analysis showed that PA-TDI duration was a feasible predictor for cardiac events in patients with CHF.

Conclusion: Long PA-TDI duration was associated with poor cardiac prognosis. PA-TDI duration is a feasible predictor for cardiac events in patients with CHF.

P1534 | BEDSIDE
Decreased left atrial mechanical function assessed by echocardiographic free strain in patients with uncontrolled blood pressure
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Purpose: Both uncontrolled blood pressure (BP) and left atrial (LA) enlargement are commonly observed in patients who receive antihypertensive agents, but the impact of uncontrolled BP on LA mechanical function remains unknown.

Methods: This study enrolled 279 hypertensive patients (HTgp) being treated and 42 normal controls. Patients were divided into the controlled (systolic BP <140 and diastolic <90mmHg, HTgp1) and uncontrolled (HTgp2) group according to their office BP readings in the past 3 months. LA function was assessed by 2-dimensional speckle tracking free strain imaging, including systolic (SSa), early diastolic (SEa) and late diastolic (SAa) strain.

Results: The 3 groups were matched with age and gender. Despite similar LA empty fraction, the hypertensive groups had significantly reduced SSa, SEa and SAa, in addition to larger left ventricular (LV) mass index and LA volume index. However, the left ventricular function (LVEF) of HTgp1 and HTgp2 (both observed in 113 (41%) patients with 47 (32%) in HTgp1 and 66 (50%) in HTgp2) was not related to the LA volumetric parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>HTgp1</th>
<th>HTgp2</th>
<th>HTgp1 vs. HTgp2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP, mmHg</td>
<td>122±12</td>
<td>138±16</td>
<td>127±10</td>
<td>150±12</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>76±8</td>
<td>82±10</td>
<td>79±8</td>
<td>87±10</td>
</tr>
<tr>
<td>LV mass index, g/m²</td>
<td>70±12</td>
<td>105±21</td>
<td>94±17</td>
<td>110±19</td>
</tr>
<tr>
<td>LA volume index, ml/m²</td>
<td>31.7±4.8</td>
<td>42.8±8.0</td>
<td>41.0±7.5</td>
<td>43.1±8.5</td>
</tr>
<tr>
<td>LA empty fraction, %</td>
<td>61.0±7.0</td>
<td>62.0±8.4</td>
<td>63.0±7.9</td>
<td>63.5±8.9</td>
</tr>
<tr>
<td>SSa, %</td>
<td>53.1±10.1</td>
<td>38.5±8.0</td>
<td>36.6±7.8</td>
<td>35.1±8.3</td>
</tr>
<tr>
<td>SEa, %</td>
<td>31.2±7.6</td>
<td>18.5±7.1</td>
<td>19.9±8.3</td>
<td>17.2±6.3</td>
</tr>
<tr>
<td>SAa, %</td>
<td>21.8±5.4</td>
<td>17.6±4.2</td>
<td>17.6±3.9</td>
<td>17.9±4.5</td>
</tr>
</tbody>
</table>

Comparison: *p<0.001, *p<0.01, *p<0.05, compared with the control group.

Conclusions: Hypertension is associated with early impairment of LA mechanical function detected by novel echocardiographic parameters. Further decrease in LA reservoir and conduit function as reflected by SEa would be attributed to the worsening of diabetes or hyperlipidemia, LV hypertrophy and LA volume index were not related with the SEa impairment.

P1535 | BEDSIDE
Redefining the size of the left atrium: matching volume and area

Left atrium (LA) size is an important predictor of adverse events in many cardiac
diseases. To estimate the LA size, volume rather than area measurements are preferred. However, using volume and area data frequently yield different assessment of the degree of LA enlargement according to the reference values published. The aim of this study was to redefine the cut-off values of LA area based on the volume measurements as the 'gold standard'.

Methods: We prospectively enrolled 357 consecutive patients referred for an echocardiogram. The LA volume indexed to BSA was calculated with the area-length biplane technique. In 256 patients, new reference area values were obtained that better correlate to the volumetric assessment using ROC analysis. In the remaining 101 patients, these new reference values were validated.

Results: Patients age range was 16–95 years. LA volume could not be measured in 14% of the patients. An agreement study between LA volume and apical 4 chamber (A4Ch) area was performed showing (weighted kappa = 0.48, 95% CI 0.42–0.54) the inaccurate classification provided by LA area values. The new reference values obtained for LA A4Ch area were: Normal = <18 cm², mildly dilated 18–20 cm² (AUC=0.85, 95%CI 0.78–0.92), moderately dilated 20–23 cm² (AUC=0.81, 95%CI 0.68–0.95), severely dilated ≥ 23 cm² (AUC=0.87, 95%CI 0.79–0.98). In 101 patients, we applied these new range values for LA area and found an excellent agreement with volume measurements (weighted kappa=0.84, CI 0.77–0.91).

P1536 | BESIDE
Tissue doppler imaging assessment of atrial mechanical delay and dysynchrony to predict non-valvular atrial fibrillation recurrence 6 month after cardioversion

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Background: Atrial mechanical dysfunctions following ST-elevation myocardial infarction (STEMI) using tissue Doppler imaging (TDI).

Purpose: To evaluate the existence and determinants of LA systolic and electromechanical dysfunction in the patients with left atrial regional deformation analysis in the patients with atrial fibrillation (AF) analyzed by tissue Doppler imaging (TDI) and using regional peak systolic velocities, compared with left atrial volume measurements. TDI-derived LA and RA velocities were measured using the regional (LVA+), posterior (vertical view between left and right pulmonary veins) and septal wall of the LA. Strain-time curve were obtained from onset of p-wave on electrocardiogram.

Results: In the bottom and lateral wall, the strain showed negative monophasic pattern (peak LS: 15±1.7%, 18±1.9%, respectively). In the posterior wall, 3 phases pattern, positive-negative-positive strain time curve was observed (peak LS: 16±9%). It seems to be the opposite of global LA strain time curve. On the other hand, peak LS was positive in the anterior and septal area (12±6%). Furthermore, in the subjects with low volume area (LVA<1.5 m²), posterior (vertical view between left and right pulmonary veins) and septal wall of the LA. Strain-time curve were obtained from onset of p-wave on electrocardiogram.

Conclusions: The regional LA deformation may be non-uniformly distributed over the whole LA, in which bottom and lateral wall may work as a systolic booster, septal and G2 area may work as passive deformation area. Furthermore, posterior LA passive deformation may get worse as LA volume was reduced, probably reflecting endocardial fibrosis accumulation.
sic volume changes. LA systolic dysfunction is associated with longitudinal left ventricular systolic dysfunction. No LA electromechanical abnormalities were detected among post STEMI patients.

P1539 | BEDSIDE
Assessment of transesophageal echocardiography to describe left atrial appendage morphology
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Purpose: Left atrial appendage (LAA) morphology, investigated by computed tomography (CT) and magnetic resonance imaging (MRI), has recently proved to relate to the risk of cerebrovascular events in patients with Atrial Fibrillation (AF). Aim of our study was to assess transesophageal echocardiographic (TEE) imaging in describing LAA morphology.

Methods: Two hundred consecutive patients referred for TEE were enrolled. In the first group of 47 (23.5%) patients LAA morphology was analyzed by conventional TEE and described as Cactus, Chicken Wing, Windscock or Cauliflower. In the second group of 153 (76.5%) patients, instead, a 3D-Xplane diagnostic algorithm, instead, significantly increased interobserver agreement up to $\rho=0.32$ within all readers and up to $\rho=0.82$ among the experienced and specifically trained operators. LAA morphology description in this latter group provided very strong agreement with cardiac MRI (up to $\rho=0.77$).

Results: By conventional TEE the agreement among operators on LAA morphology classification was poor ($\rho=0.13$). The 3D-XPlane diagnostic algorithm, instead, significantly increased interobserver agreement up to $\rho=0.32$ within all readers and up to $\rho=0.82$ among the experienced and specifically trained operators. LAA morphology description in this latter group provided very strong agreement with cardiac MRI (up to $\rho=0.77$).

Conclusions: LAA morphology assessment is challenging by conventional TEE. To improve diagnostic accuracy the use of the 3D-Xplane technique associated with a specific diagnostic algorithm and training of the operators is fundamental.

P1540 | BEDSIDE
Determinants of discrepancies between two-dimensional echocardiographic methods for assessment of left ventricular function
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Purpose: The determinants of discrepancies among 2D echocardiographic methods for assessing left ventricular function were poorly investigated. Thus we aimed at identifying the determinants of differences between two-dimensional (2D) echocardiographic methods for the estimation of LAV.

Methods: LAV was measured in 613 patients (age 45±20 years, 62% male, 282 healthy subjects, 180 athletes and 151 hypertensives) using the ellipsoid model (LAV-Ell), and the single-plane and biaxial area-length method (LAV-AL) and Simpson’s rule (LAV-Simp). Based on a mathematical model, two LA geometry indexes were also tested as predictors of discrepancies in multivariable analysis: the ratio between left atrial (LA) medial-lateral diameter in the 4-chamber view (MLD) and LA anteroposterior diameter (APD); and the ratio between 4-chamber view LA area and that of an ellipse with the same diameters (deviation from ellipse [DE] coefficient).

Results: LAV-Ell underestimated biaxial LAV-AL and biaxial LAV-Simp by an average of 35% and 26%, respectively. The MLD/APD ratio and the DE coefficient were the strongest predictors of relative differences between biaxial and the ellipsoid methods, together accounting for 76% of the difference between LAV-AL and LAV-Ell and 68% of that between LAV-Simp and LAV-Ell. The DE coefficient was also the only determinant of the LAVAL/LAVim difference ($p=0.167$, $R^2=0.001$). Body mass index (BMI) was the strongest predictor of the differences between the single-plane and the biaxial approach to the single-plane ($p=0.427$, $p=0.001$) and Simpson methods ($p=0.424$, $p=0.0001$). The concordance between single-plane and biaxial approaches was suboptimal in overweight-to-obese individuals.

Conclusions: LA geometry is the main determinant of inconsistencies between 2D methods for LAV estimation. BMI is the strongest determinant of differences between single-plane and biaxial approaches. These findings suggest that on a single-patient basis, different 2D echocardiographic methods cannot be used interchangeably for diagnosis over time, and that such methods should be preferred, particularly in overweight-to-obese individuals.

P1541 | BEDSIDE
Prognostic value of left atrial size and function assessed by three dimensional speckle tracking analysis
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Background: Several left atrial volume and functional indices calculated by 2 and 3-dimensional echocardiography have been proposed as predictors of future cardiovascular events. However, most studies have not assessed in large number of patients.

Methods: The LAV in LAVmax/LAVmin, left atrial emptying fraction (LAEmf) and LAef were measured by 2-dimensional echocardiography (2DE) and 3DE in 358 patients with various cardiovascular diseases. After excluding patients with atrial fibrillation / flutter and mitral valve disease, 321 subjects (male 68%, mean age:72±18y) were followed to determine major adverse cardiovascular events (MACE). To determine the cut off values, the same indices were measured in index 80 normal subjects.

Results: During a mean follow-up of 2.3 years, MACE developed in 76 patients, including 26 cardiac deaths. The cut-off criteria of LAVmax/LAVmin and LAEmf by 2DE and 3DEBA had significant predictive power of MACE (HR: 2.86, 95%CI: 1.55–4.86 and HR:2.78, 95%CI: 1.44–4.78). Both LAVmin and LAEmf by 3DEBA had additive predictive value for prediction of MACE over LAVmax by 3DEBA and other 2D indices.

Conclusions: LAVmin and LAEmf by 3DEBA had strong prognostic values for future major cardiac events in patients with various cardiovascular disease.

P1542 | BEDSIDE
Prognostic value of cardiac time intervals measured by tissue Doppler imaging (TDI) M-mode echocardiography in the General Population
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Purpose: The cardiac time intervals are intimately related to cardiac function and disease. Color Tissue Doppler Imaging (TDI) M-mode through the mitral leaflet is an easy, fast, and precise method to estimate the cardiac time intervals. The purpose of this study was to evaluate the prognostic value of the cardiac time intervals in predicting major cardiovascular events (MACE) in the general population.

Methods: Within the Copenhagen City Heart Study, a large community based population study, cardiac function was evaluated in 1,915 participants by both conventional echocardiography and by TDI. The cardiac time intervals, including the isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT), and the ejection time (ET) were obtained by TDI M-mode through the mitral leaflet. IVCT, ET, IVRT/ET and the myocardial performance index (MPI=(IVRT+IVCT)/ET) were calculated.

Results: During follow-up (median 10.8 years), 383 (20%) participants reached the combined endpoint (MACE) of being admitted with ischemic heart disease (IHD), heart failure and cardiac death. All the cardiac time intervals were significant predictors of future MACE (P<0.001 for all) in a compelling risk Cox regression model. However, after multivariable adjustment for clinical predictors (age, gender, BMI, eGFR, Heart Rate, systolic BP, hypertension, diabetes, smoking status, atrial fibrillation, previous IHD, previous ischemic stroke) and conventional echocardiography (LVEF, LA dimension, LVM, E/e’ only) the combined indexes, including information on both the systolic and diastolic performance (the IVRT/ET and the MPI), remained significant prognosticators (IVRT/ET: HR 1.16 (1.00-1.34), P=0.045; MPI: HR 1.12 (1.01-1.23), P=0.031). In addition, when adding the MPI to a Cox model already including all other echocardiographic parameters (LVEF, E/e’, E/A-ratio, Dec time, LA dimension, LVM), MPI resulted in a significant increase in the Harrell’s c-statistics (76.2% vs. 75.8%, P=0.048). Furthermore, reclassification analysis when adding the MPI to our clinical predictors and LVEF

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yielded a better predicting model with a significant increase in the categorical net reclassification index of 4.694% ([95% CI 2.085-7.303%), p < 0.001).

Conclusion: In the general population, the combined cardiac time intervals which include information on both the systolic and diastolic function in one index (IVRT/ET and MPI) are powerful and independent predictors of future MAC. In addition, the further prognostic information over and above clinical variables and conventional echocardiographic measures of systolic and diastolic function.

CONTRAST IMAGING AND TISSUE CHARACTERISATION

P1544 | BEDSIDE
Deformation imaging reflects myocardial histological and molecular changes in low-gradient aortic stenosis
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University of Kassel, Kassel, Germany, 2 Hannover Medical School, Hannover, Germany, 3 University of Tübingen, Tübingen, Germany, 4 University Medical Center Robert-Koch-Platz, Berlin, Germany, 5 University Hospital Jena, Jena, Germany

Purpose: Low-grade aortic stenosis (LGAS) is associated with a worse prognosis and high operative risk compared to aortic stenosis (AS) with normal left ventricular (LV) ejection fraction (EF). We aimed to find correlations between echocardiographic parameters of regional myocardial LV function and histological and molecular markers of LGAS.

Methods: Intraoperative biopsies were obtained from 5 consecutive patients with LGAS (EF 31±6%) and 7 patients with AS (EF 57±7%). Preoperative echocardiography quantified LV global and regional function. The fraction of cardiac interstitial volume (FIV) was measured using a semi-automated algorithm, the systolic volume fraction of myocardium and myofiber diameters were determined by light microscopic morphometry. Expression of sarcoplasmic-endoplasmic reticulum calcium ATPase SERCA-2a and of natrium/calcium exchanger NCX-1 were assessed by immunohistochemical staining.

Results: A significant increase in interstitial fractional volume distinguished LGAS (28.6±19.7%) from AS (10.1±7.7%) (p<0.05), without differences in myofiber diameters and myofibrillar volume fraction. At protein level LGAS was characterized by a decrease in SERCA-2a (1.7±0.45 for LGAS vs. 2.79±0.27 for AS, p<0.05) and a marked increase in NCX-1 (2.6±0.22 for LGAS vs. 0.36±0.38 units for AS, p<0.05). Echocardiographically a typical impairment of radial LV function was found in LGAS, as shown by the values of mean LV strain (7.5±2.22% for LGAS vs. 18.5±1.5% for AS, p<0.05) and respect- tively longitudinal function parameters were impaired in both groups. Significant linear correlations were found between SERCA-2a and both longitudinal (r=0.93, p<0.05) and between interstitial volume fraction and mean LV radial strain (r=0.67, p<0.05).

Conclusions: The hallmark of LGAS as compared to AS with normal EF was the delay in radial LV function due to myocardial remodeling by increased interstitial volume and compromised myocardial energetics reflected by depletion of SERCA-2a and overexpression of NCX-1. Thus, deformation imaging allows a clinically promising insight into pathogenesis of LGAS.

P1545 | BEDSIDE
Usefulness of contrast enhanced transesophageal echocardiography to guide thoracic endovascular aortic repair (TEVAR) procedure
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Background: Thoracic endovascular aortic repair (TEVAR) is commonly consid- ered as a valid alternative to surgery. Endoleaks occurrence is one of the principal limitations of TEVAR. Transesophageal echocardiography (TEE) is often adopted in adjunct to fluoscopy and angiography (ANGIO) during stent-graft implantation. In the present study we compare intraprocedural ANGIO, TEE, and contrast enhanced TEE (cTEE) and we also evaluate their accuracy in early endoleaks detection and characterization.

Methods and results: 54 patients with thoracic aortic disease suitable for TEVAR were prospectively enrolled in the study. After stent placement, the result of the procedure was assessed by ANGIO, TEE, and cTEE. The use of contrast (Sonovue, Bracco) significantly improved TEE quality (p=0.0001). cTEE was superior in entry tears, false and true lumen and aneurysm thrombosis identification, and microtears and ulcer like projections detection before stent deployment. After stent deployment, cTEE was more accurate than TEE and ANGIO in the detect- ion of slow flow in the false lumen and in the aneurismal sac (p=0.0001), and in the remaining flow identification (p=0.0001). Notably cTEE was more accurate in the endoleaks detection (p=0.0001) and in the incomplete stent expansion diagnosis and need for a further balloon inflation (p=0.002), or a further stent implantation (p=0.006), when compared to TEE and ANGIO.

Conclusions: TEVAR procedures are improved by complimentary use of contrast fluoscopy, multiplane TEE with Doppler flow interrogation, and cTEE. This triple imaging approach adds diagnostic additional information in all phases of the procedure improving safety of stent-grafting and, thus, eventually the procedural outcomes.

P1546 | BENCH
Ultrasound-enhanced thrombolysis of platelet-rich thrombi in a flow tubing system
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Background: Although diagnostic ultrasound with high mechanical indexes is able to mechanically induce clot reduction in the presence of microbubble in fusion, there have been no studies of the efficacy of sonothrombolysis for the platelet-rich thrombi (white thrombus). Therefore, the aim of the study was to demonstrate the feasibility of high mechanical indexes diagnostic ultrasound with microbubbles infusion to enhanced thrombolysis of the platelet-rich thrombi inside a flow tubing system.

Methods: Platelet-rich thrombi were formed by infused 0.4 ml of platelet-rich plasma into the tubing (diameter 5 mm). A 1.5 mm diameter needle was placed at the center of the clot and removed after thrombus formation to allow flow in- side the thrombus. A total of 36 platelet-rich thrombi were randomized to 15 minutes treatments with ultrasound (Siemens Sequioa c512, MI 1.9) and 0.5% lipid-encapsulated microbubbles (flow rate 20 ml/min) (US+MB group), ultrasound alone (US alone group) or microbubble alone (MB alone group). Ultrasound mon- itored of the lumen diameter was observed. Percentage thrombus dissolution (%) was calculated by weighing the thrombi before and after treatment.

Results: HE staining confirmed the platelet-rich thrombus formation. Lumen di- ameters were significantly diluted with US+MB treated group than the US alone group and MB alone group (13.2±1.5 mm2 vs 9.1±1.1 mm2 vs 7.6±0.9 mm2, re- spectively, p<0.05). %TD was also significantly higher with US+MB treated group than the US alone group and MB alone group (47% vs 26% vs 18%, respectively, p<0.05).

Conclusions: Thrombus dissolution of the platelet-rich thrombi was observed in a flow tubing system with high mechanical indexes diagnostic ultrasound and microbubbles.

P1547 | BENCH
Functional and volumetric left atrial reverse remodeling after cardiac resynchronization therapy: relationship with clinical response
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Introduction: Left ventricular (LV) reverse remodeling has been used to define a favourable response to cardiac resynchronization therapy (CRT). Left atrial (LA) reverse remodeling post CRT and its relation with clinical response has not been fully studied. Objective was to evaluate functional and volumetric LA remodeling and its relation with clinical outcome.

Methods: 70 patients in sinus rhythm who received CRT were included. In all patients, echocardiography was performed at baseline and 12 months follow-up with LA deformation analysis during active atrial contraction by strain derived from speckle tracking (LASa), LA negative peak strain curve during atrial contraction (LAAP). Patients were grouped according to LV reverse remodelling response as ECHO+ (LV end-systolic volume reduction>15% at 12 months) or ECHO- and to clinical outcome after CRT as Clin+ (>20% increase in the 6 minutes walking test without transplant implantation or death at 12 months) or Clin-.Paired and independent T-test were used.

Results: Globally, LA volume did not change and LASa increase after 12 months with CRT. These changes differed according to ECHO+ and Clin+ (Figure). Among patients with ECHO-, those with Clin+(n=25) showed larger increase of LASa and greater reduction of LA volume than patients with Clin-(n=15, p=0.04; TVolume AI:+6.5±7.6mL vs +13.2±14.1mL, p=0.01). Patients who were ECHO+ and Clin+ showed signifi- cantly higher LASa and a significantly lower volume at baseline as compared to other groups (Fig. 1).

Conclusions: Patients without LV reverse remodeling but with clinical improve- ment showed LA volumetric and functional remodeling post CRT. These data sug- gest that CRT has also a positive impact on LA function, which in turn contributes to the improvement of symptoms.
P1549 | BEDSIDE
Prediction of contractile reserve based on neuronal network analysis of myocardial texture in resting native and contrast-enhanced echocardiographic images
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Aim: Myocardial viability is a clinically important parameter characterizing myocardial infarction after acute coronary syndromes. It is currently defined utilizing imaging with inotropic stimulation (dobutamine stress, DSE) or structural imaging (late enhancement by CMR). Contractile reserve demonstrated by stress echocardiography is a valuable specific finding related to left ventricular (LV) recovery in long term and translating onto more favorable clinical course. We aimed to apply myocardial texture analysis using neuronal networks to predict contractile reserve in DSE in unenhanced and contrast-enhanced myocardial images acquired 7 days after percutaneous revascularization.

Methods: Apical echocardiographic views (native or contrast-enhanced with iv Sonovue injection imaged with Contrast Perfusion Sequence, CPS) were recorded in 49 pts (16 female, mean age 60±10.5) with first STEMI treated with successful primary percutaneous coronary intervention. Each pt underwent a standard low-dose DSE with dobutamine up to 15 mcg/kg/min and 40 mcg/kg/min to identify the viability in area subtended by intact-related-artery, defined as 1 grade contractile improvement (4-grade kinesia scale, 18 segment LV model). A custom software (MaZDa 4.7.7) was used for texture analysis. Briefly, 299 image features were calculated for defined regions of interest in each image (including 9 features from histogram, 6 from gradient matrix, 20 from run length matrix, 220 from co-occurrence matrix, and 44 from wavelet transform). 8 most reproducible parameters were selected based on lowest intra class feature variance followed by selection of parameters that minimized 1-nearest neighbour (1-NN) classification error.

Results: Multilayer perceptron neural network (MLP neural network based) and support vector machines (SVM, using both linear and radial basis kernels) were applied to predict the presence of segmental contractile reserve in DSE. Neuronal network (MLP) and SVM in native resting echocardiogram achieved 80% accuracy. In area-at-risk prediction was correct for 69% (native) and 68% (CPS, red component), better than results obtained with SVM (correct classification for 68% and 62%, resp.

Conclusions: Texture analysis with advanced computational tools including SVM and MLP allows for 70% accurate prediction of contractile reserve in DSE of infarct-related segments, a slightly less than obtained in previous research for prediction of necrosis thickness in CMR but offering an alternative for predicting this parameter in native resting echocardiogram.

P1549 | BEDSIDE
Effects of glucagon-like peptide-1 (GLP-1) on myocardial blood flow reserve in diabetes, cardioprotection or not? A study in type 2 diabetes and non diabetics under controlled glycemic conditions
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Background: We evaluated the effect of glucagon-like peptide-1 (GLP1) on myocardial blood flow reserve (MBFR) in subjects with & without type 2 diabetes (T2D & non-T2D) under controlled glycemic conditions.

Methods: 21 subjects with no CAD [8 T2D & 13 non T2D] underwent 2 visits (GLP1 visit: GLP1 infusion at 1.2 pmol/kg/min & Normal Saline (NS) visit: NS infusion]. During each visit, 2 stage pancracl pump (somaticatolin, glucagon and insulin) was infused, along with glucose to maintain euglycemia followed by hyperglycemia (each 2 hr stages). Blood glucose (BG) was monitored 10 min. Myocardial contrast echocardiography (MCE) was performed during final 30 min of steady glycemic state using Definity (200 ml/hr) at rest & during reagdenosin stress [400 ug iv bolus]. MBFR was quantified.

Results: Non-T2D (85% females, age 48±6 yrs, BMI 25±3 kg/m2,fasting BG 90±5 mg/dL, HbA1C 5.3±2%), T2D (75% male, age 54±6 yrs, BMI 32±4 kg/m2, fasting BG 143±22 mg/dL, HbA1C 7.1±7%). BG levels across groups (T2D-GLP1, T2D-NS, non-T2D-GLP1, non-T2D-NS) during euglycemia were (94±5, 96±5, 98±3, 94±8 mg/dL, 236), while hyperglycemia (103±13, 238±11, 228±11 mg/dL, P=0.055, respectively. Mean hyperglycemic MBFR was reduced vs euglycemic MBFR in T2D-NS, P=0.038 & non-T2D-NS, P=0.031, but not in T2D-GLP1 or nonT2D-GLP1. Figure. For both glycemic stages, MBFR was lower in T2D-NS vs non-T2D-NS (euglycemia p=0.010; hyperglycemia p=0.003), but was not different in T2D-GLP1 vs nonT2D-GLP1 (euglycemia p=0.125; hyperglycemia p=0.048). T2D-NS showed trend for lower hyperglycemic MBFR vs T2D-GLP1, p=0.059.

Conclusions: MBFR is lower in euglycemic T2D than nonT2D.Hyperglycemia reduces MBFR in both diabetics and nonT2D.GLP-1 infusion appears to modulate MBFR, is lower in euglycemic T2D than nonT2D. GLP-1 infusion appears to modulate MBFR.

P1550 | BEDSIDE
Prognostic role of dobutamine stress contrast echo in coronary artery disease: how does age interrelate to appropriateness criteria?
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Purpose: Dobutamine stress contrast echo (DSCE) is a valuable adjunct in clinical practice for the assessment of the presence and extent of coronary artery disease (CAD). The aim of the current study was to evaluate the prognostic role of DSCE in patients with known or suspected CAD in different age groups according to appropriateness indication.

Methods: We studied 2380 (58±9 years) consecutive patients who were referred to our department for DSCE. Patients were classified into 3 groups according to their age: young adults (age <45yrs), middle-aged (45±45yrs) and hospitalizations. Furthermore, they were stratified according to the 2011 appropriateness criteria as appropriate (A), uncertain (U) and inappropriate (I). Mean follow-up lasted 57±1.1±1.0 months. End points included all-cause mortality, cardiac death, the need for late revascularization (-3 months) and hospitalizations.

Results: Out of 2380 patients, 45.6% were classified as appropriate, 31.7% as inappropriate and 22.7% as uncertain. In (20.6%) patients, ischemic response to DSCE was illustrated. During follow-up end-points were noted in (9.9%) patients. Moreover, appropriate and uncertain setting combined was more predictive for a positive DSCE result than the inappropriate class (p= 58.8%, p<0.05), with the most positive response being noted in the appropriate setting (28.1%). Logistic regression analysis revealed that DSCE response was the strongest predictor for adverse outcomes (OR 51.7, p<0.05), especially for middle-aged patients.

P1551 | BENCH
The NFKB binding motif promotes nuclear import of plasmid DNA and improves the efficiency of ultrasound-targeted microbubble destruction mediated gene transfection
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Purpose: As a novel non-viral gene delivery system, ultrasound-targeted microbubble destruction (UTMD) appears to be a promising technology. However, the transfection efficiency was not desirable. The nucleic complexes need to be responsible for the inefficiency because they restrict the import of exogenous genes. So in this study we tried to improve the nuclear import of plasmid DNA using the NFκB binding motif and increase the transfection efficiency of UTMD.

Methods: Human umbilical vein endothelial cells (HUVECs) were transfected using UTMD with two different gene labeled plasmids: psHD1-uHNFκB. The plasmid was constructed by inserting a specific DNA targeting sequence (five optimal repeats of the binding motif for the inducible transcription factor NFκB) into the psHD1-uHNFκB. Cell Counting Kit-8 (CCK-8) was used to test the effect of NFκB binding motif on cell viability. The nuclear distribution of SF1-uHNFκB was tested using fluorescence microscope. The expression level of SF1-IκB was detected by RT-PCR, Western Blot and ELISA. The nuclear import and gene expression efficiency of SF1-uHNFκB were detected and compared with those of psHD1-uHNFκB to explore the effect of NFκB binding motif on gene transfection.

Results: The insertion of NFκB binding motif did not affect cell viability. The nuclear import and gene expression of psHD1-uHNFκB were significantly higher than the negative control plasmid.
P1553 | SPOTLIGHT

Diagnostic value of strain echocardiography, galactin-3 and tenasin-c levels for the identification of patients with pulmonary and cardiac sarcoidosis

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Background: Cardiac involvement in sarcoidosis has been associated with poor prognosis. We evaluated myocardial contractility quantitatively in a cohort of pulmonary sarcoidosis (PS) patients with and without cardiac involvement. We also studied markers of fibrosis (tenasin-C [Tn-C] and galectin-3 [Gl-3]) as diagnostic tools for PS and cardiac sarcoidosis (CS).

Methods: Forty ambulatory patients with PS of grades 1–2, and 26 healthy subjects were prospectively enrolled. All patients with PS underwent cardiac magnetic resonance (CMR) to explore the presence of CS. The study population was divided into three groups: controls (n=26), non-CS patients (n=34), and CS patients (n=6). Speckle-tracking strain echocardiography (STE) was performed on all patients, and Gl-3 and Tn-C values measured in all patients and controls.

Results: PS patients had higher levels of Gl-3 and Tn-C than did controls, and the STE parameters of PS patients, including global longitudinal strain (GLS) and global circumferential strain (GCS), were lower than those of controls (p<0.001 for all comparisons). GLS values were lower in CS patients than in the other groups (p=0.05).

Conclusion: Patients demonstrate reduced cardiac contractility, independent of CMR-proven structural cardiac lesions, while patients with structural lesions have more pronounced drop in strain parameters. Tn-C and Gl-3 are promising markers for the diagnosis of PS, but they are not specific for cardiac involvement.

ASSESSMENT OF LEFT VENTRICULAR FUNCTION BY 3D ECHOCARDIOGRAPHY

P1555 | BEDSIDE

Comparison of three-dimensional and two-dimensional global longitudinal strains of left ventricle in patients with acute myocardial infarction


Background: Global longitudinal strain of left ventricle (GLSLV) is an objective parameter of global myocardial function. Three-dimensional echocardiography is a theoretically ideal in the measurement of LV mechanics. We want to compare GLSLV by 3-dimensional strain echocardiography (GLSLV-3D) and 2-dimensional strain echocardiography (GLSLV-2D) in patients with acute myocardial infarction (AMI)

Methods: From September 2011 to April 2013, all consecutive patients with first AMI were included. GLSLV were calculated with 3-D and 2-D speckle tracking with EchopAC-PC software (GE medical systems). Mean clinical follow-up was 17.6 months for checking adverse clinical events including heart failure admission, AMI and death.

Results: Total 142 patients (111 males, mean 61±12 years old) were analyzed. Of them, 101 patients (71%) were diagnosed as ST-segment elevation myocardial infarction. GLSLV-3D had significant correlations with GLSLV-2D (r=0.490, p<0.001), 3-D LV ejection fraction (LVEF-3D, r=−0.496, P<0.001), wall motion score index (WMSI, r=−0.354, P<0.001) and NT pro-B-natriuretic peptide level (r=−0.323, P<0.001). There were 9 major adverse clinical events (2 deaths, 6 hospitalizations for heart failure, and 1 AMI) during the follow-up period. GLSLV-3D was associated with adverse clinical events (HR=1.335, 95% CI=1.063-1.676, P<0.013). However, GLSLV-2D did not show significant result (HR=1.143, 95% CI=0.943-1.389, P=0.172).

Conclusions: GLSLV-3D showed good correlations with GLSLV-2D, LVEF-3D, WMSI and serum NT pro-BNP concentration. GLSLV-3D was associated with significantly adverse long-term adverse clinical events in patients with AMI.

P1556 | BEDSIDE

Relation between left ventricular diastolic elastance and myocardial deformation indices

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Background: Diastolic elastance (Ed) which is the ratio of mitral inflow and annular velocity to stroke volume (E/e’/SV) has been proposed as a marker of ventricular diastolic properties. Our aim was to assess the relations between Ed and myocardial mechanical parameters using three dimensional speckle tracking echo-cardiography (3DSTE).

Methods and results: We studied 54 normal subjects (mean age 35±12.3 years, 54% males, LVEF: 58.6±3.1%). Arterial elastance (Ea) as approximated by the ratio of end-systolic pressure (ESP) to SV; end-systolic elastance (Ees) calculated as the ratio of ESP to end-systolic volume and ventricular-arterial coupling (VAC), the ratio of Ea/Ees were calculated. Myocardial mechanical parame-
P1557 | BEDSIDE

Left ventricular contractile function in hypertension assessed by myocardial global strain rate using novel one-beat three-dimensional speckle tracking echocardiography with high volume rate

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Background: Left ventricular (LV) systolic properties in hypertension (HTN) are impaired by pressure overload, resulting in heart failure (HF) with reduced ejection fraction (HFEF). LV myocardial strain rate (SR) during systole evaluated by 2D STE was reported as a quantitative index of LV contractility. However, the heart is a complex organ that undergoes cyclic changes in multiple directions and the mechanics seem to be best represented by 3D strain tensor. Thus, we examined LV contractility by global SR using a novel one-beat real-time 3D-STE with high volume rate and assessed the hypothesis that LV contractility in HTN is already reduced before LV EF or SW among 5 groups (LV EF: control; 67 ± 9%, B; 69 ± 9%, C; 68 ± 5%, D; 0.8 ± 0.3 s⁻¹, *p < 0.05). LV SR during systole in all 3 directions reduced in HTN with B, C and D compared with control (longitudinal strain: control; -19 ± 4%, B; -26 ± 5%, C; -28 ± 5%, D; -14 ± 5%, *p < 0.05). LV SR during systole in all 3 directions reduced in HTN with B, C and D compared with control (radial strain: control; 2.6 ± 0.5, A; 2.4 ± 0.5, B; 2.1 ± 0.5, C; 2.0 ± 0.3 D; 1.7 ± 0.3 s⁻¹, *p < 0.01) despite no reduction in LV EF and SW among 5 groups (LV EF: control; 67 ± 5, A; 66 ± 6, B; 67 ± 5, C; 68 ± 9 and D; 67 ± 9% and SW: control; 4.4 ± 1.0, A; 4.4 ± 1.0, B; 4.4 ± 1.0, C; 5.1 ± 1.2 and D; 5.4 ± 1.6 kg m⁻¹, *p < 0.05), LV SR during isovolumic contraction also reduced in HTN with hypotrophy (radial SR: control; 1.2 ± 0.4, A; 1.1 ± 0.3, B; 1.0 ± 0.3, C; 0.8 ± 0.3 s⁻¹, *p < 0.01) and correlated negatively with LV mass (r = -0.31, p < 0.01).

Conclusions: LV contractility in HTN with hypotrophy assessed by global myocardial SR during systole and isovolumic contraction using the novel 3D-STE algorithmly reduced without reduction in LV EF and SW. LV global SR during systole and isovolumic contraction is a sensitive marker of contractility and may be useful to detect an early phase of HFEF.
was performed by a third investigator without knowledge of the results of the 3DE analysis.

Results: Bland-Altman analysis showed that EDVs measured using semiautomated algorithms with manual editing were significantly more accurate than those measured with fully automated algorithms (bias = -16 ml, LOA ± 35 ml and bias = -31 ml, LOA ± 41 ml, p < 0.0001 for EF, and bias = -19 ml, LOA ± 37 ml, bias = -0.42 ml, p < 0.0001 for SC 2000, respectively). Conversely, end-systolic volumes (ESV) and EF were similar with both fully automated and semiautomated algorithms. As expected, fully automated algorithms reduced the time to EDV (r = -0.92, p < 0.0001) and improved inter-observer reproducibility (bias ± LOA) in comparison with semiautomated algorithms with manual editing both using EDV: EDV (1.8 vs 1.22 ml, respectively), ESV (1.2 vs 1.7 ml), EF (1.5 vs 1.8%) (all p < 0.01); and SC 2000: EDV (1.16 vs 6.30 ml), ESV (0.13 vs 0.10%) (all p < 0.05).

Conclusions: Fully automated 3D algorithms for LV quantification are time-saving and improve inter-observer reproducibility of LV volume measurements. However, they provide LV EDVs which are significantly less accurate than semiautomated ones in comparison with CMR, therefore the LV stroke volume is underestimated using fully automated 3D algorithms.

P1560 | BEDSIDE

Noninvasive estimation of left ventricular diastolic function in hypertension by novel one-beat real-time three-dimensional speckle tracking echocardiography with high volume rate

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Background: Left ventricular (LV) pressure overload in hypertension (HTN) causes LV hypertrophy (LHV), which leads to decline of LV relaxation and increase of LV stiffness. LV myocardial strain rate (SR) during isovolumic relaxation (IVR) measured by 2-dimensional speckle tracking echocardiography (2D-STE) was reported to have a good correlation with time constant of LV pressure decline (tau). However, the heart is a complex organ that undergoes cyclic changes in multiple dimensions, the mechanics seem to be best represented by 3D strain tensor. Thus, we developed a novel one-beat real-time 3D-STE and software to measure global myocardial SR and examined LV diastolic function in HTN.

Methods: Patients with HTN (n=85, age 69±7) and preserved ejection fraction (EF) (= 50% and controls (n=60, age 69±9) were enrolled. Patients with HTN were divided into 4 groups according to LV geometry (A: normal geometry, n=21: B: concentric remodeling, n=20: C: concentric LVH, n=24 and D: eccentric LVH, n=20). We measured LV longitudinal, circumferential and radial global SR during IVR as LV relaxation by the novel 3D-STE with high volume rate of 50-80fps. We estimated LV stiffness as LV diastolic stress / LV strain. LV stiffness was calculated as LV diastolic radius x PCWP / end diastolic wall thickness. PCWP was measured by a third investigator without knowledge of the results of the 3DE analysis.

Results: There was no difference in LVEF among 5 groups. LV mass was increased in HTN with hypertrophy compared to control (C: 133±26 and D: 132±16 vs. control:88±14g/m2, p < 0.01). LV radial SR during IVR in HTN was decreased compared with control (54 ± 15 vs. 64 ± 15 p < 0.05). LV circumferential and radial SR were decreased in HTN compared to control (52 ± 15 vs. 61 ± 15, p < 0.01). There was a significant correlation between LV mass and SR during IVR in all directions (radial: r=0.30, p < 0.01).

Conclusions: LV relaxation even in HTN with normal geometry assessed by LV global myocardial SR during IVR using the novel 3DE was already impaired despite no reduction of LVEF and no elevation of E/e'. LV stiffness was increased in only HTN with LHV. Noninvasive evaluation of LV diastolic function using SR by 3D-STE may be useful to detect an early phase of heart failure with preserved EF.

P1561 | BEDSIDE

Intervendor consistency and accuracy of left ventricular volume measurements using three-dimensional echocardiography

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Purpose: Intervendor consistency and accuracy of 3DE L V volume measurements from 3 different systems (i.e., E9, Philips Medical System, Andover MA; Vivid E9, GE Vingmed, Horten, N; Acuson SC2000, Siemens, CA) during the same echo session. CMR was performed in 35 patients. A single researcher analyzed the 3DE data sets with QLABs (Philips Medical System), E9 (GE Medical System, Andover, MA) and SC2000 (Siemens, CA) in row one week apart from one vendor to the others. CMR quantification of LV volumes was performed by a second investigator.

Results: All 3 3DE systems provided LV volumes which were closely correlated with CMR volumes: EDV (E9: r=0.92, bias -15 ml, LOA ±42 ml; E9: r=0.96, bias -16ml, LOA ±35 ml; SC 2000: r=0.94, bias -19 ml, LOA ±41 ml), end-systolic volume (E9: r=0.93, bias -11 ml, LOA ±42 ml; E9: r=0.98, bias -15 ml, LOA ±35 ml; SC 2000: r=0.95, bias -11 ml, LOA ±39 ml), and EF (E9: r=0.86, bias 1, LOA ±13%); E9: r=0.84, bias 3, LOA ±15%; SC 2000: r=0.84, bias 0, LOA ±15%); 3DE LV volumes and EFs measured with E9 and E9 in the 71 study patients were similar (Table). Conversely, LV EF was significantly lower when measured with SC 2000 (Table, data are summarized as median 95% CI).

LV volumes and EF among the 3 3DE system

<table>
<thead>
<tr>
<th>System</th>
<th>EDV (ml)</th>
<th>ESV (ml)</th>
<th>LVEF (%)</th>
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<tr>
<td>E9</td>
<td>143 (133,159)</td>
<td>150 (131,169)</td>
<td>0.276</td>
</tr>
<tr>
<td>SC2000</td>
<td>144 (133,159)</td>
<td>150 (131,169)</td>
<td>0.276</td>
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</tbody>
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Conclusions: We showed a good agreement between 3DE and CMR using the three tested echo systems, whereas LV EF was underestimated by SC 2000. Our results may help in the interpretation of 3DE volumes obtained using different 3DE systems.

P1562 | BENCH

Prediction of treatment response for cardiac resynchronization therapy by left ventricular twist using three-dimensional speckle tracking imaging in a heart failure canine model

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Objective: To assess left ventricular (LV) twist by three-dimensional speckle tracking imaging (3D-LSI) in a paced induced heart failure canine model with left bundle-branch block (LBBB) undergoing cardiac resynchronization therapy (CRT). Methods: After induction of left bundle branch block by radiofrequency ablation, rapid right ventricular pacing (RVP) at 200 beats/min was utilized in 22 adult beagle dogs for 6 weeks to induce heart failure. Then 15 dogs received CRT for 4 weeks and others were treated as control. Apical full-volume acquisition of the LV was obtained in conscious animals at baseline, the end of 6-week RVP and the end of 4-week CRT. Peak LV systolic twist (Ptw) and torsion (Ptor) along with peak apical and basal rotation were automatically calculated by Tom-Tec 4D LV Analysis 3.0 software to identify the ideal parameter in predicting treatment response of CRT. Results: After 4 weeks of CRT, LVEF increased ([31.97 ± 6.06] vs. [37.47 ± 6.30]%, p < 0.002) and LVESV decreased ([24.13 ± 3.73] vs. [21.87 ± 3.15] ml, p < 0.007) significantly in dogs with heart failure by shortening the duration of basal rotation [(23.73 ± 20.5) vs. (17.87 ± 5.94) ms, p < 0.009]. CRT improved peak LV systolic twist [6.06 ± 0.99 (9.03 ± 0.63)*, p < 0.008] and torsion [(12.10 ± 0.36) vs. (9.88 ± 0.39)*, p < 0.010] compared with peak apical (5.97 ± 0.57) vs. (6.13 ± 0.61)*, p < 0.010) and basal rotation [(2.08 ± 0.45) vs. (2.13 ± 0.48)*, p = 0.469]. CRT treatment response, defined as improvement of LVESV ≥ 15%, was observed in 9 dogs. Significant difference was found in Ptw ([7.43 ± 0.61] vs. [6.06 ± 0.89]*, p < 0.016) and Ptor ([1.43 ± 0.45] vs. [0.67 ± 0.36]*, p < 0.042) between responders and nonresponders. The cut-off values derived from receiver-operating characteristic curve analysis were 6.73* for Ptw and 1.00* for Ptor with satisfying sensitivity as 89% and 85%, specificity as 83% and 84%, respectively. Conclusions: CRT improved LV systolic twist and reversed LV remodeling by reconciling basal with apical rotation. Peak twist and torsion evaluated by 3D-STE demonstrated potential predictive value for treatment response of CRT.
in 45 patients and non-specific conduction delay (NSCD) was in 30 patients. Activating imaging studies were performed with a 3D-STE system (Toshiba Medical Systems) in addition comprehensive echocardiographic examinations. The images were obtained with more than 30 volume/sec. The regional myocardial deformation was assessed by the area tracking method. Regional myocardial activation was defined as onset of regional contraction, which was corresponding to the timing at 20% of the maximum regional strain value. The activation imaging allowed visualizing propagation of myocardial activation, which were analyzed before and 7 days after CRT. In addition, the regional time from QRS onset to activation was measured, and the intra-ventricular propagation time (IVPT) was calculated as the time difference between the first and latest activated segments.

Results: We found 5 propagation patterns as follows; 1) U-shaped activation pattern in which initial activation site was observed at mid septum and propagated around apex and to the basal lateral region in 36 LBBB and 3 NSCD patients, 2) direct propagation pattern from septum or anterior to lateral wall in 7 LBBB and 3 NSCD patients, 3) regional conduction delay pattern in 2 LBBB and 8 NSCD patients, 4) multi-directional delay pattern in 10 NSCD patients, and 5) no apparent propagation delay in 6 NSCD patients. IVPT in the pattern 1 to 4 did not differ, which were longer than the pattern 5. CRT responders defined as ≥ 15% reduction of left ventricular end-systolic volume at 6 months after CRT were observed in 34 (90%) with the U-shaped activation pattern, however, only 9 (25%) patients in each of 2 and 5. In 5 CRT non-responders with U-shaped activation pattern, 4 patients showed LV pacing site estimated by activation imaging was located at the 2 or more remote segments from the latest segment before CRT.

Conclusion: Intra-ventricular propagation pattern analysis by 3D-STE derived activation imaging was useful to identify CRT responders, rather than quantification of intra-ventricular dyssynchrony. In addition, activation pattern analysis after CRT also may provide additional information about CRT responses.

P1564 | BEDSIDE
Assessment of 3D left ventricular function and 3D speckle tracking echocardiography: comparison to 2D planimetry and 2D speckle tracking
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Purpose: Three dimensional speckle tracking (3DS), measuring longitudinal, radial, and circumferential myocardial deformation, might constitute a more accurate and comprehensive approach to the evaluation of 2D planimetric speckle tracking (2DS). We sought to compare the results of 3DS to those measured by 2DS analysis in patients with preserved left ventricular ejection fraction (LVEF) and chronic heart failure (CHF).

Methods: In an ongoing study, transthoracic echocardiography was performed in 52 consecutive patients, comprising standard apical 4-, 2-chamber- and long axis views. LVEF was defined as onset of regional contraction, which was determined by the combination of four ECG-gated subvolumes. Differences of left ventricular (LV) diameter, LV mass, cardiac index, average global longitudinal systolic strain (GLPS), and TAPSE were calculated by using the Wilcoxon or Mann-Whitney-U test; differences of p < 0.05 were considered significant. After creation of a scatter plot for 2D / 3D GLPS, correlations between the 2DS and 3DS method were tested by the Spearman-Rho correlation coefficient.

Results: Out of the 52 patients, 27 had a preserved and 25 a reduced LVEF due to ischemic or dilated cardiomyopathy. LVEF was 62.5% in healthy controls (<21.2% vs. -17.1% and 9.5% vs. 8.3%, respectively). Also, LVEF was significantly reduced in the 3DS method compared to 2D biplane planimetry. Inter- and intra-observer variability was low (<10%).

Conclusions: 3DS and 3D assessment of left ventricular function provided significantly lower strain values in all subgroups. 2DS and planimetry might overestimate the actual spatial myocardial movement due to its inability to track the twist- ing, 2-dimensional myocardial displacement, resulting in a "pseudo-shortening" of the heart. On the other hand, temporal and spatial resolution of 3DS is limited compared to the high-frame rate 2DS. Despite the numerical differences, however, 3DS correlated significantly with the more established 2DS analysis and seems to constitute a promising new method to investigate myocardial systolic function.

P1565 | BEDSIDE
Noninvasive activation imaging using three-dimensional speckle tracking echocardiography in wolf-parkinson-white syndrome
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Background: We have developed activation imaging with 3-dimensional speckle tracking echocardiography (3D-STE), which allows visualizing the wave front image of mechanical activation propagation.

Methods: Sixteen patients with manifest Wolf-Parkinson-White (WPW) syndrome were imaged with 3D-STE activation imaging mode, which aims to quantify a time from the onset of electrical activation to the onset of regional deformation. To visualize the timing of regional mechanical activation, if a regional endocardial area change ratio (ACR) value exceeded 25% of maximum ACR value in each 16 segment of the left ventricle, the area was colored by a colour corresponding to the time from QRS on the polar map image. 3D-STE for left ventricle, which was constructed by 6-beats, results in time resolution of 33 msec. An analyzer who was unaware of the clinical information assessed the accessory pathway location by both Arruda electrocardiogram (ECG) criteria and by 3D-STE.

Results: ECG and 3D-STE determined that the preexcitation sites were perfectly consistent in 7 patients with 14 sites of different ventricle activation in 2 and 6 patients, and inconsistent in 7 and 3 patients, respectively. Among 3 patients of inconsistent with the preexcitation site evaluated by 3D-STE, ECG correctly assess the ablation site in 2 patients.

Conclusions: The activation imaging with 3D-STE may be the promising noninvasive imaging tool to localize preexcitation sites in patients with WPW syndrome, especially in conjunction with the standard ECG assessments.

P1567 | BEDSIDE
Variability in global longitudinal strain measurements between different vendors: Where do we stand? The EACVI-ASE-Inter-Vendor Comparison Study
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Background: Two-dimensional speckle-tracking-based global longitudinal strain (GLS) is a new echocardiographic parameter for the assessment of left ventricular (LV) function. Different methodological approaches, however, prevent the comparability of measurements obtained with ultrasound systems of different vendors. The European Association of Cardiovascular Imaging and the American Society of Echocardiography together with all major ultrasound system vendors have therefore initiated a task force to standardize GLS measurements. This study was initiated to test the inter-vendor variability of GLS measurements in a clinical setting.

Methods: In a unique setting with 7 different ultrasound systems in one room, 434 echocardiographic examinations were performed in 62 volunteers with normal and abnormal cardiac function. Apical 4-, 2-chamber and long-axis views were obtained, with image settings optimized for speckle tracking GLS according to recommendations of the respective vendor. In order to determine inter-observer variability, a set of apical images was taken by a second sonographer. Then, another set of apical images was taken by the first sonographer in order to determine test - re-test variability of GLS measurements. All vendors provided dedicated software to measure GLS on data sets obtained with their machines. Additionally, two independent software vendors were tested. Variability in GLS measurements were compared between vendors and with measurements of LV ejection fraction (EF; biplane Simpson’s method), transmural E velocity and E/A ratio, LV end-diastolic diameter and LV interventricular septum (IVS) and posterior wall (PW) thickness. The results from 8 vendors are presented here.

Results: Significant differences between vendors were found in GLS measurements (P<0.001, ANOVA). The mean GLS from all vendors was 19.4%. The mean of each vendor differed from the mean of all vendors by a range of -2.1 to 1.5%. The interobserver mean error was 5.7-9.1% (relative percentage), while the respective value was for EF 9.5%, for E 12.7%, for E/A 20.7%, for LVED 7.9%, for IVS thickness 11.6% and for PW thickness 17.6% (P<0.001, ANOVA). The intraobserver mean error was 5.4-7.6% for GLS, while for EF it was 7.6% (P<NS).

Conclusion: Significant differences between vendors were found in LV GLS. Intraobserver variability was low and better compared to EF and standard echocardiographic parameters, while interobserver variability was comparable to EF.
Evaluation of left ventricular endocardial and epicardial performance in hypertension assessed by the novel one-beat real-time three-dimensional speckle tracking echocardiography

M. Arai1, T. Noda2, S. Watanabe2, S. Minatoguchi1.

There was no difference in LV ejection fraction among 5 groups. LV SR ejection fraction and normal wall motion score.

Background: LV rotation and torsion have been known as important speckle tracking echocardiographic (STE) parameters of LV systolic function in HTN. The left ventricular (LV) rotation and torsion have been known as important speckle tracking echocardiographic (STE) parameters of LV systolic function in HTN. We investigated the feasibility of LV rotation and torsion in the early stage in proportion to the degree of LVH rather than those at epicardium, contractility by SR during systole at endocardium in HTN deteriorated even in the posterior wall. According to gender, septal s' peak wave velocity and isovolumic contraction (IVC) peak velocities and durations at the level of healthy population (n=734; 45.8±7) and 60 normal controls (age: 69±6, LV mass: 88±14g/m²). Patients with HTN were divided into 4 groups according to LV geometry (A: normal geometry, LV mass: 92±13g/m², B: concentric remodeling, 97±12g/m², C: concentric LVH, 133±26g/m², D: eccentric LVH, 132±15g/m²).

Results: There was no difference in LV ejection fraction among 5 groups. LV SR at both myocardial layers could be measured within 3 minutes by the novel 3D-STE with volume rate of 65±5psv. LV radial SR during isovolumic relaxation at endocardium in HTN was significantly decreased compared to normal despite no reduction of SR at epicardium. (Figure)

Methods: LV SR during isovolumic relaxation as LV relaxation and SR during systole as contractility at both endocardium and epicardium were measured by the 3D-STE in 85 patients with HTN (age: 69±7) and 60 normal controls (age: 69±6, LV mass: 88±14g/m²). Patients with HTN were divided into 4 groups according to LV geometry (A: normal geometry, LV mass: 92±13g/m², B: concentric remodeling, 97±12g/m², C: concentric LVH, 133±26g/m², D: eccentric LVH, 132±15g/m²).

Purpose: LV rotation and torsion are feasible to investigate subclinical myocardial function. LV rotation is feasible to investigate subclinical myocardial function.

Conclusions: LV relaxation assessed by SR during isovolumic relaxation and contractility by SR during systole at endocardium in HTN deteriorated even in early stage in proportion to the degree of LVH rather than those at epicardium, suggesting that LV endocardial ischemia and dysfunction may be caused by LV hypotrophy. The novel 3D-STE will be useful tool to examine the myocardial layer function in HTN.

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Differences in Tissue Doppler Imaging parameters of left ventricular systolic function according to gender and age in healthy subjects

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Purpose: Systolic Tissue Doppler Imaging (TDI) parameters are complementary tools in the evaluation of left ventricular (LV) systolic function, especially in patients with subtle systolic dysfunction despite preserved LV ejection fraction. Whether these parameters are influenced by gender and age has not been previously addressed in a large cohort of patients. We aim to report the differences in these parameters according to gender and age and provide normal reference ranges in healthy subjects.

Methods: The NORRE study is a multi-centre study involving accredited laboratories of the EACVI studying echocardiographic parameters in a large cohort of healthy population (n=734; 45.8±13.3 years; 43.6% of male). We evaluated s' wave and isovolumic contraction (IVC) peak velocities and durations at the level of the mitral annulus in the walls. Isovolumic acceleration (IVA) was calculated as the ratio of IVC peak velocity and time to peak velocity of IVC. TDI index was calculated according to current knowledge. All the parameters were analyzed according to gender and age (20-40; 40-60; >60 years).

Results: S' peak velocity was significantly higher in younger patients in all the walls except in the inferior wall (Table). A significant correlation was found between age and s' peak wave. According to gender, septal s' wave peak velocity was higher in male (9.0 vs. 8.4; p=0.045), without significant differences in the rest of the walls. Regarding IVA, no differences were found according to age and genders. No differences were found in the TDI index according to age, except in the posterior wall, where TDI index was higher in older patients (0.44 vs. 0.48 vs. 0.56; p=0.009). TEI index in the inferior wall was higher in men compared with women in the inferior wall (0.45 vs. 0.40; p=0.039).

S' waves velocities according to age

<table>
<thead>
<tr>
<th>Parameters</th>
<th>20–40 yrs</th>
<th>40–60 yrs</th>
<th>&gt;60 yrs</th>
<th>All</th>
<th>p-value</th>
<th>Correlation with age</th>
<th>r</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S' septal (cm/s)</td>
<td>9.5±1.4</td>
<td>8.5±1.4</td>
<td>7.9±1.2</td>
<td>8.6±1.4</td>
<td>0.033</td>
<td>−0.244</td>
<td>0.013</td>
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<tr>
<td>S' lateral (cm/s)</td>
<td>11.5±2.6</td>
<td>9.9±2.1</td>
<td>8.9±3.0</td>
<td>10.5±2.7</td>
<td>0.001</td>
<td>−0.429</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>S' anterior (cm/s)</td>
<td>9.9±1.5</td>
<td>9.3±1.7</td>
<td>8.9±1.7</td>
<td>9.5±1.6</td>
<td>0.011</td>
<td>−0.205</td>
<td>0.082</td>
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</tr>
<tr>
<td>S' posterior (cm/s)</td>
<td>10.5±1.9</td>
<td>9.1±2.2</td>
<td>8.9±2.2</td>
<td>9.8±2.1</td>
<td>0.016</td>
<td>−0.343</td>
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<tr>
<td>S' posterior (cm/s)</td>
<td>11.1±1.6</td>
<td>9.6±1.5</td>
<td>9.4±2.7</td>
<td>10.3±1.9</td>
<td>0.003</td>
<td>−0.401</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Normal reference values for s'peak velocity should be used according to age categories given the influence of age in this parameter.

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Increased carotid artery stiffness in coronary artery disease assessed by speckle-tracking and its good association with aortic stiffness and endothelial dysfunction


Aim: (i) evaluate carotid artery strain derived from speckle-tracking ultrasound imaging (STE) in subjects with coronary artery disease (CAD) and without coronary artery disease (N-CAD), (ii) compare CAS, to global aortic stiffness using carotid-femoral pulse wave velocity (c-f PWV) and to endothelial function using brachial flow-mediated dilatation (FMD) in subjects with CAD.

Methods: From March 2012 to January 2013, we consecutively enrolled patients with significant CAD. Significant CAD was defined as more than 70% of diameter stenosis on coronary angiography. Patients were divided into CAD group and control group. Patients with depressed LV systolic function and abnormal regional wall motion abnormality were excluded.

Results: We analyzed total 182 subjects. 70 patients were female, mean age was 65.9±9.7 years old. Total 110 patients were included in CAD group, and 72 patients of CAD group were diagnosed as acute coronary syndrome. LV ejection fraction (LVEF) on echocardiography was no significant difference between control group and CAD group. (60.3±5.9 vs. 61.5±5.9, p=0.485, respectively) However, there were statically significant differences of LV torsion, apical rotation between control group and CAD group (Table 1).

<table>
<thead>
<tr>
<th>Control group (n=72)</th>
<th>CAD group (n=110)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular torsion (degree)</td>
<td>22.8±4.9</td>
<td>19.5±6.8</td>
</tr>
<tr>
<td>Apical rotation (degree)</td>
<td>14.4±6.2</td>
<td>11.9±5.8</td>
</tr>
<tr>
<td>Basal rotation (degree)</td>
<td>−8.8±4.5</td>
<td>−8.3±4.9</td>
</tr>
<tr>
<td>4 chamber longitudinal strain (%)</td>
<td>−20.9±2.8</td>
<td>−19.1±2.3</td>
</tr>
<tr>
<td>2 chamber longitudinal strain (%)</td>
<td>−20.9±2.1</td>
<td>−19.3±2.4</td>
</tr>
<tr>
<td>3 chamber longitudinal strain (%)</td>
<td>−20.5±2.1</td>
<td>−19.4±2.3</td>
</tr>
<tr>
<td>Global longitudinal strain (%)</td>
<td>−20.2±1.8</td>
<td>−19.3±2.1</td>
</tr>
</tbody>
</table>

Conclusion: Patients with significant CAD and normal LV systolic function have lower LV torsion and apical rotation. These findings could be helpful to understand subclinical myocardial dysfunction in patients with significant CAD, LV torsion and apical rotation is feasible to investigate subclinical myocardial function.
Methods: 100 subjects were prospectively included, and classified into 2 groups: subjects with CAD (CAD, n=49), subjects N-CAD (N-CAD, n=51). The CAS on the common carotid artery using speckle-tracking ultrasound imaging was measured. In the CAD, c-f PWV and FMD were evaluated and compared to CS.

Results: Age: The proportion of males, diabetes, and a history of CAD was higher in the CAD group (2.41% vs 4.48%, p < 0.0001). In CAD group, 41% presented stabled angina and 59% acute coronary syndrome (ACS). The CAS was inversely correlated to c-f PWV (r=-0.7, p=0.0001) and correlated with endothelial dysfunction (r=0.45, p=0.003).

Conclusion: Speckle-tracking ultrasound imaging is a non-invasive and useful tool for the evaluation of the local carotid artery stiffness. Carotid artery stiffness was impaired in coronary artery disease. In CAD, carotid artery stiffness measured by speckle-tracking is associated with global aortic stiffness and endothelial dysfunction.

P1574 | BEDSIDE
Flow mapping in ventricular aneurysms: a tool to predict the probability of thrombus development
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Introduction: Adverse remodeling after myocardial infarction includes the potential development of ventricular aneurysms. These segments with no contractility are occasionally associated with the development of thrombi. However, indications on the need for antithrombotic treatment in these patients is not well established given the absence of data to assess the risk of thrombus development. The purpose of this study is to analyze the factors associated with the presence of intra-aneurysmal thrombi as a first approach to the possibility to predict its development.

Methods: Patients with intraventricular aneurysm underwent echocardiographic examination with Vector Flow Mapping (VFM), an advanced echo-modality capable of depicting and quantifying complex intracardiac flow patterns. Flow characteristics and wall shear stress in the aneurysmal area were analyzed using a series of mathematical calculations derived from VFM imaging mode.

Results: 11 patients (10 males, aged 70.6 ± 10.5 years) were studied. Three of them (27%) presented a thrombus in the aneurysmal region. Patients with intra-aneurysmal thrombus presented significant differences with those with no thrombus: peak velocity of flow entering the aneurysm was decreased (5.9 ± 0.8 cm/s vs. 9.3 ± 2.7 cm/s, p < 0.05), they had no reverse flow towards the apex during systole (0% vs. 75%, p < 0.05) and maximum wall shear stress in the aneurysmal wall, graded on a 0-to-5 scale, was reduced (1.67 vs. 4.50, p < 0.001).

Conclusions: The study of ventricular aneurysms with flow mapping tools provides information on flow behavior that may be relevant to discriminate patients at risk of developing intra-aneurysmal thrombus and who may, therefore, benefit from antithrombotic therapy.
Purpose: Pulmonary hypertension (PHTN) is defined by a mean pulmonary artery pressure (mPAP) ≥ 25mmHg at rest measured at right heart catheterization (RHC). Tracing the spectral Doppler signal in aortic stenosis is a recognized, reliable, and reproducible method of estimating the mean pulmonary pressure across the valve. We aimed to determine if the same principle of tracing the tricuspid regurgitant (TR) continuous wave spectral Doppler signal would provide a more physiologic and representative estimation of the mPAP.

Methods: The study cohort comprised PHTN patients undergoing RHC and transthoracic echocardiograms (TTE) on the same day. Only cases with TTE studies containing “complete” TR spectral Doppler signals were included. Tracing the TR signal provided the TR mean gradient (TRMG). Right atrial pressure (RAP) was estimated based on the size and collapsibility of the inferior vena cava. The mPAP by TR (mPAP-TR) was then derived as TRMG + RAP.

Results: 100 patients (85±14 years; 86% female) were included. The mPAP on RHC was 42.5±12.4mmHg and mPAP-TR was 45.9±12.2mmHg. mPAP-TR demonstrated good agreement (Intraclass correlation 0.885) and consistency (Cronbach’s alpha 0.904) with invasive RHC measurements (See attached Bland-Altman plot demonstrating a relative mean difference of 3.44±7.26mmHg). The measurement of mPAP by this technique showed excellent test-retest reproducibility (Intra-observer variability 2.4% and inter-observer variability 2.1%). The presence of a “complete” TR spectral Doppler signal to allow accurate tracing is the only technical limitation.

Conclusion: This novel non-invasive method for estimation of mPAP is useful in the assessment of PHTN severity. mPAP-TR is simple, reproducible, and correlates well with invasive RHC measurements.

HEART AND STROKE

P1575 | BEDSIDE
Relation between cryptogenic ischemic stroke and patent foramen ovale in young and middle-aged adults in northeastern China
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Purpose: To compare the prevalence of PFO in young and middle-aged patients with cryptogenic ischemic stroke (CS) and in normal population in northeastern China.

Methods: Our case-control study included consecutive 318 young and middle-aged patients with CS (36±8 years old, ranged from 18 to 50, 135 women) and 336 normal control subjects with matched age and sex (36±7 years old, ranged from 19 to 50, 139 women) for group comparisons. Stroke risk factors including hypertension, diabetes mellitus, hyperlipidemia, ischemic heart disease, atrial fibrillation, carotid atherosclerosis plaques and smoking, etc. were studied. Transesophageal echocardiography (TEE) tests were performed to detect the presence of PFO. The prevalence of PFO and difference of risk factor levels between the groups was compared. Then the odds ratios (OR) of a PFO was estimated in CS patients versus control subjects.

Results: The prevalence of PFO was significant higher in patients with CS than in normal control subjects (145/318, 45.6% versus 46/336, 13.7%, P<0.001). The OR for PFO in CS for patients younger than 60 years old was 6.8 (confidence interval, 4.1 to 11.5). There were no significant differences in other stroke risk factors between two groups. The size of PFO was larger in stroke group than that in control group (P<0.05).

Conclusion: PFO may play an important role in etiology of CS in young and middle-aged adults. Larger and longer PFOs may be more concomitant with ischemic attacks. More efforts should be employed in patients with CS to detect PFO for further treatment.

P1578 | BEDSIDE
Anatomical characteristics of the left atrial appendage in cardiogenic stroke with low CHADS-VASc scores
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Purpose: In patients with atrial fibrillation (AF), left atrial appendage (LAA) morphology has been suggested to modify risk for embolic events. In this case-control study we tested the hypothesis that embolic risk in patients with low CHADS-VASc scores (<1) is associated with LAA characteristics.

Methods: Of 2,069 patients who underwent AF ablation, 25 (1.2%) had a prior thromboembolic event and a previously low CHADS-VASc score. Those patients were matched (1:3) for the CHADS-VASc criteria with 75 thromboembolic event-free patients and CT data were compared. LAA measurements (volume, ostium diameters, surface and circumference), morphology (cactus, chicken wing, windsock, cauliflower) and takeoff of the superior or inferior edge in relation (higher or lower) to the respective takeoff of the adjacent pulmonary vein (PV) were determined. LAA flow and heart rate from a resting ECG prior to ablation were also compared.

Results: Univariate analysis showed that patients with thromboembolic events had a higher incidence of superior LAA takeoff (i.e. higher than the left superior PV; 28% vs. 4%, p=0.002) and a higher incidence of hyperlipidemia (40% vs. 17%, p=0.028), while LAA morphologies (20% cactus, 24% chicken wing, 8% windsock, 48% cauliflower vs. 16%, 36%, 9%, 38% respectively, p=0.69), inferior takeoff (64% vs. 55%, p=0.48), and other LAA characteristics (volume: 8.8±4.9 vs. 7.8±3.3 ml, p=0.24, flow: 53.1±21 vs. 56.1±21 cm/s, p=0.51) were similar between groups. Logistic regression revealed that a superior LAA takeoff (OR: 9.1, 95% CI: 2.1 to 38.6, p=0.003) was the only independent predictor of thromboembolic events. There was a negative correlation between heart rate and LAA flow (r=-0.2 cm/s pro ml, p=0.048), that was that was even more pronounced for the superior LAA takeoff (r=-0.67 cm/s pro ml, p=0.035).

Conclusion: A higher LAA takeoff is associated with higher thromboembolic risk while LAA morphology is not. These findings may have implications for anticoagulation management of AF patients with low CHADS-VASc scores and higher LAA takeoff.

P1579 | BEDSIDE
Diastolic dysfunction in ischaemic stroke patients predict future cardiovascular events

Background and objectives: Left ventricular (LV) diastolic dysfunction is associated with major cardiovascular events including congestive heart failure (CHF), stroke, acute myocardial infarction (MI) and death. Tissue Doppler E/E’ is a non-invasive estimate of left atrial filling pressure and marker of diastolic function, has also been reported to predict primary cardiac events. In recent years, a transthoracic echocardiogram (TTE) has become standard of care in the assessment of patients who present with ischaemic strokes or transient ischaemic attacks (TIA). This study aims to evaluate the utility of tissue Doppler E/E’ as a predictor for future cardiovascular events in stroke patients.

Methods: This was a retrospective study of 229 consecutive patients who presented to our acute stroke unit with ischaemic strokes or TIA. All patients had a TTE with the ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/E’) measured. Follow up data was obtained from hospital records. Outcomes of interest at 3 years included MI, CHF and all-cause death. Data analysis was carried out using SPSS 16.0.

Results: Majority of the patients were male (n=151). 22.3% and 8.3% had prior histories of ischaemic heart disease and CHF respectively. Logistic regression analysis showed that an E/E’ of ≥ 15 independently predicted cumulative MI (17.8% vs 4.2%, p<0.004), CHF (15.1% vs 3.5%, p=0.028) and all-cause death (26.0% vs 9.1%, p<0.004) at 3 years.

Conclusions: In patients who present with an ischaemic stroke or TIA, the presence of LV diastolic dysfunction, as evidenced by an elevated E/E’, was a predictor of future cardiovascular events. This is despite the routine use of antplatelet and statin therapies in them. Further study is needed to determine whether more intensive efforts such as functional stress tests or coronary assessment/vascularization can benefit this group of patients.
The relationship between left atrial enlargement and incidence of stroke in patients with atrial fibrillation: from the Fushimi AF registry

Y. Hamatani1, D. Takagi1, M. Iuchi1, H. Ogawa1, M. Esato2, Y. Chun2, H. Wada3, K. Hasegawa1, M. Abe4, M. Akao5 on behalf of the Fushimi AF Registry investigators. 1Kyoto Medical Center, National Hospital Organization, Kyoto, Japan; 2Linkai Takeda General Hospital, Kyoto, Japan

Purpose: Atrial fibrillation (AF) is a common arrhythmic disorder and increasing incidence of Stroke is a devastating long-term complication of AF. Controversy exists regarding whether left atrial enlargement is a risk factor of stroke.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku, Kyoto, Japan. Fushimi-ku is assigned to represent a typical urban community in Japan. At present, we have enrolled 3,821 patients (4.1% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,966 patients as of December 2013. Left atrial enlargement (LAE) was diagnosed if the left atrial diameter measured by transthoracic echocardiography was >45 mm. We compared the baseline clinical backgrounds and incidences of clinical events during one-year follow-up period between those with LAE and those without it (non-LAE).

Results: Patients with LAE accounted for 41.4% of all the patients. The proportion of female was comparable between LAE group and non-LAE group (39.6% vs 40.9%; p=0.52). LAE group was older (LAE 74.8 ±10.1 vs. non-LAE 73.2 ±11.0 years; p<0.01), and had higher CHADS2 score (2.26 ±1.30 vs. 1.98 ±1.36; p<0.01). Heart failure was more in LAE group, but other major co-morbidities, such as hypertension, diabetes mellitus, and the history of stroke, were comparable. LAE group showed slightly higher, but not statistically significant, incidence of stroke during one-year follow-up, compared with non-LAE group (3.0% vs 2.0%; p=0.11). After adjustment for CHADS2 risk factors and oral anticoagulant prescription, LAE was associated with slightly higher risk for stroke (adjusted odds ratio (OR) = 1.51, 95% confidence interval (CI): 0.86 to 2.65, p=0.15). In female patients, LAE group showed significantly higher incidence of stroke during one-year follow-up (4.0% vs 1.5%; p<0.01), but this was not the case in male patients (2.3% vs 2.3%; p=1.00). In patients with CHADS2 score ≥1, incidence of stroke during one-year follow-up was significantly higher (LAE 7.5% vs 4.0%; p<0.01), whereas that was comparable in those with CHADS2 score <2 (2.9% vs 3.1%; p=0.85).

Conclusion: The Fushimi AF registry represents the clinical profile of real-world Japanese AF patients. AF patients with LAE showed higher risk profiles for stroke, such as hypertension, diabetes mellitus, and the history of stroke, were comparable. LAE group showed slightly higher, but not statistically significant, incidence of stroke during one-year follow-up, compared with non-LAE group (3.0% vs 2.0%; p=0.11). After adjustment for CHADS2 risk factors and oral anticoagulant prescription, LAE was associated with slightly higher risk for stroke (adjusted odds ratio (OR) = 1.51, 95% confidence interval (CI): 0.86 to 2.65, p=0.15). In female patients, LAE group showed significantly higher incidence of stroke during one-year follow-up (4.0% vs 1.5%; p<0.01), but this was not the case in male patients (2.3% vs 2.3%; p=1.00). In patients with CHADS2 score ≥1, incidence of stroke during one-year follow-up was significantly higher (LAE 7.5% vs 4.0%; p<0.01), whereas that was comparable in those with CHADS2 score <2 (2.9% vs 3.1%; p=0.85).

Prevalence of cardiac tumors in patients with cardioembolic stroke


Purpose: To evaluate the prevalence of intracardiac tumors in a population of patients with a cardioembolic ischemic stroke and to define their echocographic characteristics.

Methods: This noncentric, retrospective study was conducted between May 2004 and November 2012. All consecutive patients with an ischemic stroke of potential cardioembolic etiology and who underwent transcranial (TTE) and/or transesophageal echocardiography (TEE) were selected for the analysis. Intracardiac masses suspected of being cardiac tumors potentially responsible of stroke were analyzed.

Results: 2,948 patients with ischemic stroke potentially caused by cardioembolic events in 2,948 patients with ischemic stroke were selected for the analysis. Intracardiac masses suspected of being cardiac tumors potentially responsible of stroke were analyzed.

Conclusion: The relationship between left atrial enlargement and incidence of stroke in patients with atrial fibrillation: from the Fushimi AF registry

Background and purpose: Atrial fibrillation (AF) is associated with hemostatic abnormalities and increases risk of thromboembolic events. Some reports show that plasma D-dimer level is increased in patients with AF. But the relation of plasma D-dimer level to thromboembolic events in patients with AF remains unknown. We assessed 303 nonvalvular AF patients with measured plasma D-dimer level in the first medical examination and the risk of thromboembolic events in patients with AF.

Methods: We assessed 303 nonvalvular AF patients with measured plasma D-dimer level in the first medical examination and the risk of thromboembolic events in patients with AF.

Results: 95 patients incurred thromboembolic events and 208 patients were event free (31% vs 69%). An univariate analysis showed that D-dimer level ≥0.5 μg/ml (odds ratio, OR, 7.13; p=0.01) and age ≥75 years (OR, 2.9; p<0.01) were significant predictors of each factor of CHADS2 and CHA2DS2-VASc scores (OR, 5.36; p<0.01). In low CHADS2 scores (0-1), patients with D-dimer level ≥0.5 μg/ml were significantly incurred thromboembolic events compared with D-dimer level <0.5 μg/ml (80% versus 53%, p=0.02). In low CHADS2-VASc scores (0-1), the risk of thromboembolic events tended to be higher in patients with D-dimer level ≥0.5 μg/ml compared with D-dimer level <0.5 μg/ml (75% versus 39%, p=0.06).

Conclusion: AF patients with D-dimer level ≥0.5 μg/ml in the first medical examination should be treated with oral anticoagulant therapy as well as AF patients with D-dimer level ≥0.5 μg/ml.
Both scores were good predictors of embolism (CHADS2: c-statistic= 0.67; 95%CI: 0.56-0.78; p<0.005); (CHA2DS2-VASc: c-statistic= 0.75; 95%CI: 0.66-0.83; p<0.001), with CHA2DS2-VASc being superior to CHADS2 (DeLong test, p<0.01).

Annual rate of embolic events depending on thromboembolic risk

<table>
<thead>
<tr>
<th>Embolic risk (CHADS2 score)</th>
<th>Annual rate of thromboembolism (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0)</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (1)</td>
<td>1.65</td>
</tr>
<tr>
<td>High (&gt;1)</td>
<td>3.15</td>
</tr>
</tbody>
</table>

Annual rate of embolic risk (CHA2DS2-VASc score)

<table>
<thead>
<tr>
<th>CHA2DS2-VASc score</th>
<th>Annual rate of thromboembolism (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0 in males, 1 in females)</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (1 in males)</td>
<td>2.90</td>
</tr>
</tbody>
</table>

Conclusions: Both CHADS2 and CHA2DS2-VASc thromboembolic risk scores are good predictors of embolic risk in real-world NVAF patients undergoing DC cardioversion, with CHA2DS2-VASc having significantly better predictive value.

P1584 | BEDSIDE

Incidence of atrial fibrillation and subsequent medication changes in cryptogenic stroke patients with an implantable loop recorder

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Purpose: Stroke patients are at high risk of stroke recurrence. This study evaluates the risk profile, incidence of atrial fibrillation (AF), and medication changes in patients with unexplained (cryptogenic) stroke or transient ischemic attack (TIA) who underwent continuous monitoring with an implantable loop recorder (ILR).

Methods: The observational INSIGHT XT study prospectively enrolled patients who received an ILR with a dedicated diagnostic algorithm for atrial fibrillation, irrespective of the clinical indication. The study was submitted to local MECS and informed consent to participate in the study and/or for using personal data was obtained. Of 1003 patients enrolled in the study between Aug 2008 and Jan 2012, 121 received the ILR to evaluate cryptogenic stroke or TIA at 20 study centers. The definition of cryptogenic stroke/TIA was at the investigators’ appraisal and no standard approach to patient work-up was required.

Results: The median follow-up duration was 12.5 months (IQR 11.7, 13.4). The mean age of patients was 62±13 years and 47% were female. A stroke was the index event in 71%; whereas 29% had a TIA. At baseline 62% of patients had hypertension, 12% had diabetes, none had a history of heart failure, and 12% had a history of AF. The mean CHADS2 score was 2.9±1.0 and the mean CHA2DS2-VASc score 4.0±1.3. At enrollment, 93% of patients were taking antithrombotic medication and 5% were on oral anti-coagulation (OAC). AF was observed in 24 patients (20%) and the mean time to diagnosis of AF was 5.7±5.1 months. Twelve of the AF patients were started on OAC. During the study, six patients experienced a stroke or TIA (median time to event 3.6±4.6 months), of which 1 patient died.

Conclusions: We found a high proportion of patients with AF in this multicenter cohort of patients with cryptogenic stroke representing clinical practice. These patients have high CHADS2/CHA2DS2-VASc scores and physicians initiated OAC based on the available diagnostic data from continuous monitoring with the ILR.

P1585 | BEDSIDE

Impact of combination of left atrial volume index and markers of thrombogenesis on risk assessment of thrombus formation in the left atrial appendage

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Purpose: Left atrial appendage (LAA) is a major thromboembolic source in cardioembolic stroke. As shown in the Virchow’s triad, circulatory stasis, hypercoagulability, and endothelial dysfunction, are important factors for thrombus formation. The aim of this study was to investigate whether the clustering multiple noninvasive markers of thrombogenesis based on Virchow’s triad is associated with LAA thrombus formation.

Methods: We measured plasma soluble fibrin monomer complex (SFMC) as a marker of hypercoagulability and plasma von Willebrand factor (vWF) as a marker of endothelial dysfunction in 307 consecutive acute ischemic stroke patients and 168 proximal atrial fibrillation patients who underwent transesophageal and transcranial Doppler US examinations. Left atrial appendage volume (LAVI) which reflects LAA function as a marker of circulatory status.

Results: LAA thrombus was detected in 60 patients. LAVI, plasma vWF and SFMC levels were significantly higher in patients with LAA thrombus than in those without. Multivariate regression analysis revealed that LAVI and vWF are independent risk factors after adjusting confounding factors. LAVI was a much greater risk factor than vWF and SFMC. Further, the patients with increased LAVI combined with high vWF and/or high SFMC had a greater risk for LAA thrombogenesis compared to those solely with increased LAVI (odds ratio vs. no increased LAVI; increased LAVI and vWF vs high vWF and high SFMC: 52.2 ± 0.001, increased LAVI and high vWF, 33.0 ± 0.0001, increased LAVI and high SFMC, 22.9 ± 0.05, only increased LAVI, 9.6 ± 0.05, respectively).

Conclusion: Combined assessment of LAA dysfunction with hypercoagulability and endothelial dysfunction may be a reliable evaluation for LAA thrombogenesis.
Patients with CHA2DS2VASc scores ≥2 seemed to be clear candidates for anticoagulant treatment with high risk for ischemic stroke, low bleeding risk and moderate mortality rate.

Conclusions: Atrial fibrillation patients with aspirin had a clinically relevant risk of ischemic stroke regardless of CHA2DS2VASc scores, but also a higher rate of complicating co-morbidities, more serious bleeds and substantially higher mortality rate.

PERCUTANEOUS CORONARY INTERVENTION IN HIGH-RISK SUBJECTS

Methods: What does the new clinical syntax score have to offer? comparison of the predictive ability of syntax score I and II in patients who underwent unprotected left main angioplasty (ULMA) as well as to evaluate the clinical impact of the SII guided revascularization strategy reclassification.

Methods and results: Single Centre retrospective analysis of 132 patients (79.5% men, mean age 65.8±12years) who underwent ULMA between March 1999 and December 2010. Both scores were calculated using the online calculator and the published SII nomogram (presupposes independent calculation for each revascularization strategy). We estimated the discriminative ability for MACES at 4 years of follow-up.

Abstract P1558 – Table 1. Outcomes among 26 937 AF patients with CHADS2VASc scores 2–9; with and without complicating baseline characteristics (dementia, alcohol abuse, renal disease, anemia, earlier severe bleeding, or frequent faits).

Table: Outcomes 2010 Warfarin Aspirin

Uncomplicated (n=10024) Complicated (n=4189) Risk ratio Uncomplicated (n=6551) Complicated (n=6173) Risk ratio

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Warfarin Risk ratio</th>
<th>Aspirin Risk ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke</td>
<td>2.0 (1.7–2.3)</td>
<td>2.1 (1.6–2.5)</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0.5 (0.4–0.6)</td>
<td>0.9 (0.5–1.2)</td>
</tr>
<tr>
<td>Traumatic intracranial bleeding</td>
<td>0.3 (0.2–0.4)</td>
<td>0.6 (0.3–0.8)</td>
</tr>
<tr>
<td>Any severe bleeding</td>
<td>1.9 (1.6–2.2)</td>
<td>3.8 (3.2–4.4)</td>
</tr>
<tr>
<td>Deceased (all cause)</td>
<td>2.9 (2.6–3.3)</td>
<td>6.2 (5.6–6.9)</td>
</tr>
</tbody>
</table>

Kaplan-Meier for incidence of stroke.

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P1592 | BEDSIDE
GRACE score predicts short- and long-term mortality but overestimates the mortality risk in ACS patients treated with PCI of LM stenosis

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Aim: The purpose of the study was to assess mortality in ACS patients with significant left main coronary artery (LMCA) stenosis treated with PCI and to evaluate GRACE score as a predictor of immediate and long-term results.

Results: 269 ACS patients treated with PCI LMCA were included in the study. There were 105 STEMI and 146 NST-ACS patients with infarct/symptom-related left anterior descending artery or left circumflex artery respectively and accompanying significant LMCA stenosis, and 18 patients with symptom-related LMCA. Mean age was 65.8 years. Low LV EF (-35%) was in 41% patients. The mean GRACE score was 179.9. The mean SYNTAX score was 31. In-hospital mortality for the whole group was 3.0%. The mean follow up period was 51 months. Long-term mortality appeared to be 6.7%. NST ACS group had the lowest mortality (2.1%). Long term mortality in STEMI patients and LMCA-symptom related group 16.2% and 33.4% respectively. GRACE score higher that 179.9 was considered to be an independent risk factor of in-hospital (OR=2.1, p=0.004) and long-term mortality (OR=2.8, p=0.002). However, the observed mortality was much lower than predicted with GRACE (3.0% vs 8.0% respectively, p=0.01). The differences between observed and predicted mortality were significant in groups of patients, divided in respect to the GRACE score percentile (fig. 1). Predicted 6-months mortality with the use of GRACE score at discharge (mean 113.4) was 12%, but the observed mortality during the follow up period appeared to be much lower (6.7%).

Conclusions: GRACE score is an important tool in assessing short- and long-term prognosis in patients with ACS treated with PCI of LMCA, but it overestimates the mortality rate.

P1593 | BEDSIDE
Increasing incidence, atypical risk factor profile and excellent long-term outcomes of young patients treated with primary PCI for ST-elevation myocardial infarction

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Introduction: There have been a number of studies focusing on the relationship between age and outcome following Primary Percutaneous Coronary Intervention (PPCI) for ST-elevation myocardial infarction (STEMI). However, the majority of these studies have focused on outcomes in elderly patients. Our aim in this study was to compare the characteristics and outcomes of young patients undergoing PPCI in those of older patients.

Methods: This study was an observational study of 3618 patients with STEMI treated by PPCI between January 2004 and September 2012 at a large PPCI centre. We compared the outcome in young patients (<45 age) with older patients (>45 age). The primary endpoint was long-term mortality with long-term major adverse cardiac events (MACE) as a secondary endpoint. Median follow-up was 3.0 years (IQR range: 1.2-4.6 years).

Results: Of the 3618 STEMI patients, 367 (10.14%) were young patients and 3251 (89.9%) were older patients. Over the follow-up period, rates of mortality (2.7 vs. 7.6; p=0.0001, Figure 1) and MACE (7.0% vs. 13.5%; p=0.0001) were significantly lower in the young group compared to the older group. After adjustment for confounding variables using multivariate analysis, young patients had lower all cause mortality when compared with older patients (HR 0.12 [95% CI: 0.04-0.38]), including after incorporation of a propensity score (HR 0.14 [95% CI: 0.04-0.36]).

Conclusions: Our data suggests that younger patients are accounting for an increasing proportion of patients treated by PPCI for STEMI. These patients are more likely to be male smokers of South Asian origin with LAD disease than older patients, but to have fewer other conventional risk factors. Furthermore, these patients have favourable in-hospital, intermediate and long-term outcomes after PPCI.

P1594 | BEDSIDE
Combined and independent impact of diabetes and chronic kidney disease among patients undergoing percutaneous coronary intervention for chronic total occlusion: results from a single center study


Purpose: Diabetes mellitus (DM) and chronic kidney disease (CKD) are independent predictors of poor outcomes following percutaneous coronary intervention (PCI) and are associated with complex coronary disease, including chronic total occlusions (CTO). While CTO recanalization may improve outcomes, the impact of CTO PCI in patients with and without DM and CKD remains unclear.

Methods: We performed a retrospective analysis of 887 consecutive patients undergoing CTO PCI between 2009 and 2012. We compared clinical and angiographic characteristics in patients stratified by the presence or absence of DM and CKD (DM and CKD (DM and CKD = 105, DM only= 289, CKD only=124 and neither=369). We assessed 1-year clinical outcomes and mortality in each subgroup.

Results: Patients with DM and CKD were older with more multi-vessel disease and severely calcified lesions. PCI success rates were lower among those with DM and CKD (61.4%) or CKD alone (62.1%), compared with DM alone (70.4%) and patients with neither condition (74.1%) (p<0.01). While 1-year overall MACE outcomes were not significantly different between groups, all-cause mortality was highest among those with DM and CKD (Figure).

Conclusion: Successful recanalization of CTO lesions is less common among patients with both DM and CKD compared to those with neither or one condition. Excess mortality risk even after successful PCI suggests that CTO PCI should be approached with extreme caution in this unique, high risk cohort.

P1595 | BEDSIDE
Mortality trends after unprotected left main stem percutaneous coronary intervention in England, 2005-2010: Analysis of 5,063 cases from the British Cardiovascular Intervention Society (BCIS) registry

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Purpose: To report temporal trends in the treatment and outcomes after UPLMS PCI according to presentation by ST-elevation myocardial infarction (STEMI), non-STEMI, and unstable angina (UA).
ST-elevation acute coronary syndrome (NSTEACS) and chronic stable angina (CSA).

Methods: Prospective population-based linked cohort study of 5,065 patients from the BCIS database, 1st Jan 2005 through 31st Dec 2010.

Results: From 2005-6 to 2009-10, STEMI UPLMS PCI cases increased from 10.5 to 18.7%, on the other hand NSTEACS and CSA cases decreased: 48.9 to 45.8% and 40.6 to 35.4% respectively. Mean (SD) age was 69.6 (11.8) years for STEMI, 69.9 (12.1) years for NSTEACS and 70.6 (12.5) years for CSA. There was a preponderance of males in all years. Overall baseline risk increased; cardiacogenic shock: 7.7 to 12.2%, P=0.001; severe left ventricular systolic dysfunction, 14.9 to 17.3%, P<0.001; age >80 years, 20.9 to 26.0%, P=0.035. Radial PCI increased from 17.6% in 2005-6 to 40.5% of cases. Compared with 2005-6, 30-day mortality in 2009-10 was stable (STEMI: adjusted odds ratio (aOR), 95% confidence interval (CI) 0.9, 0.5 to 1.4; NSTEACS 0.9, 0.6 to 1.4; CSA 0.9, 0.2 to 3.4). Likewise, 1-year mortality remained stable (STEMI aOR 0.8, 95% CI 0.5 to 1.4; NSTEACS 1.1, 0.8 to 1.5; CSA 1.7, 0.9 to 3.0). For STEMI with cardiacogenic shock, 30-day and 1-year mortality rates decreased by 17.4% (95% CI, 13.4 to 21.9%) and 16.6% (12.4 to 21.3%) reaching 44.0% and 43.9% in 2009/10, respectively.

Results: From 2005-6 to 2009-10, STEMI UPLMS PCI cases increased by 2-fold between 2005 and 2010. Baseline risk increased and across all groups to early and late mortality was stable. Although mortality rates for STEMI with cardiacogenic shock declined, they remained high.

Conclusions: In England, the number of cases of UPLMS PCI increased by over 2-fold between 2005 and 2010. Baseline risk increased and across all groups to early and late mortality was stable. Although mortality rates for STEMI with cardiacogenic shock declined, they remained high.

P1597 | BEDSIDE
Effect of aspiration thrombectomy on outcomes in patients with acute myocardial infarction: an updated meta-analysis of randomized control trials

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Background: A recent meta-analysis suggested that aspiration thrombectomy during acute myocardial infarction (AMI) may be associated with lower risk of all-cause mortality and major adverse cardiac events (MACE) during a 30-day follow-up (PMID: 23665372). However, findings from the TASTE randomized controlled trial (RCT) did not confirm these findings. We conducted a new meta-analysis including TASTE data to examine the effect of aspiration thrombectomy (AT) before primary percutaneous coronary intervention (PCI) vs primary PCI alone on these outcomes.

Methods: Pre-TASE RCT (18 trials, n=3,936) and TASTE RCT (n=7,244) randomized AMI patients to PCI with or without AT. Primary outcome was 30-day mortality. Secondary outcomes including MACE, stroke, target vessel revascularization and reinfarction were also studied.

Results: All-cause mortality occurred in 2.9% and 3.4% of patients undergoing vs not undergoing AT (risk ratio {RR}: 0.86; 95% CI: 0.72-1.00; p=0.01; Fig. 1). RR for mortality for pre-TASE meta-analysis and TASTE RCTs were 0.71 (95% CI: 0.51-0.99; p=0.049) and 0.94 (95% CI: 0.72–1.22; p=0.629) respectively (Fig. 1). AT was associated with significantly lower MACE events overall (RR: 0.81; 95% CI: 0.71-0.93; p=0.002) despite no effect in the TASTE RCT (RR, 0.85; 95% CI: 0.70–1.03; p=0.101).

Summary plot comparing mortality

Conclusions: Compared with conventional primary PCI alone, PCI with manual catheter aspiration thrombectomy for treatment of AMI was not associated with lower risk for all-cause mortality. The effect of AT on MACE, though significant, is inconsistent with that from the largest and most recent TASTE RCT (52% weight) and need to be interpreted with caution.

P1598 | BEDSIDE
Predictors of coronary artery aneurysm after stent implantation in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

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Background: The clinical and angiographic predictors of coronary artery aneurysm (CAA) formation in patients with ST-segment elevation acute myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) is not clear. This study aims to assess the predictors of CAA formation after PCI.

Methods: 3428 patients who underwent PCI for STEMI were enrolled. The average period of follow-up was mean 48 months (range, 35 to 56 months) after PCI. During this time, 1304 (38%) patients were undergone follow-up coronary angiography (CAG). CAA was detected in 21 patients (1.6%). CAA occurred at the segment of stent implantation in all patients. The clinical and angiographic data were compared between patients with CAA group (n=21) and without CAA group (n=1283) (figure).

Adjusted 30-day 1-year mortality risks.

Conclusions: In contemporary PCI, the risk of adverse events after DAPT cessation was highest following disruption, intermediate with discontinuation and lowest with interruption in both groups (Fig. 1). Risk associated with disruption and discontinuation was similar in magnitude and direction across ACS strata (Fig. 1). While risk with interruption was numerically higher among ACS patients, interaction testing was non-significant (p=0.17).
Results: Patients who developed CAA had longer reperfusion time, higher high-sensitivity C-reactive protein (hs-CRP) levels and neutrophil to lymphocyte ratio (NLR) than those who had without CAA. Angiographically, CAA developed proximally located lesions and lesion length was significantly greater in patients with CAA than without CAA. Statin and betablocker discontinuation were found to be an important predictor of the diagnosis of stent-related CAA. Every 1 mg/L increase in hs-CRP and implantation of drug eluting stent (DES) were independent predictor of CAA formation after STEMI.

Conclusions: Baseline elevated inflammation status and DES implantation in the setting of STEMI may predict the CAA formation.

P1599 | BEDSIDE
Transradial access for coronary artery catheterization in the elderly: are there differences between left or right approach?
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Purpose: Transradial access for coronary interventions is being routinely used despite of limitations related with technical and anatomical issues. Elderly patients have a higher risk of access-site complications related to invasive coronary catheterization. Our purpose was to evaluate feasibility of radial access and to compare left versus right radial access in very old patients.

Methods: Retrospective study of all patients ≥80 years who underwent coronary artery catheterization through radial access at our institution. Success rate (defined as complete procedure performed through the radial access), crossover rate, fluoroscopy time, volume of contrast and diagnostic and interventional procedures were collected. Statistical analysis was performed with the SPSS software.

Results: A total of 886 patients were included (43.7% female), mean age 82.8 ± 2.6 years (range 80-90), who underwent a radial access coronary angiography. Right radial artery (RRA) was used in 770 (86.9%) and left radial artery (LRA) in 116 (13.1%). No statistically significant differences were observed in sex or type of procedure (diagnostic or intervention) between both groups. Primary success rate was 94.8%, and access crossover was required only in 47 patients (5.2%), all in the RRA group (36 patients were changed to femoral access, 10 to LRA and 1 to right cubital access). Percutaneous coronary intervention (PCI) was performed in 352 patients (39.7%). Mean fluoroscopy time showed a trend to be shorter in RRA group (11.22 ± 9.6 min vs 12.89 ± 10.04 min, p = 0.09), while the volume of contrast was significantly lower in the RRA group (132.9 ± 78.1 ml vs 153.2 ± 68.36 ml, p = 0.008). When coronary angiography and PCI were evaluated independently, fluoroscopy time was similar in diagnostic procedures (RRA 7.7 ± 6.7 ml, LRA 8.8 ± 4.5 ml, p = 0.23) but the volume of contrast was significantly lower in the RRA group (95.2 ± 53.9 ml vs 122.1 ± 51.4 ml, p = 0.01). PCI patients showed no significant differences either in fluoroscopy times (RRA 17.1 ± 11.4 min, LRA 17.8 ± 12.4 min, p = 0.72) or in volume of contrast (RRA 189.9 ± 79.8 ml, LRA 190 ± 67.7 ml, p = 0.98).

Conclusions: In this series of elderly patients, transradial access success rate was high, suggesting that radial access is safe and feasible in daily practice in patients ≥80 years. LRA approach was not associated with a significant reduction in fluoroscopy time compared to the RRA approach (even showed a trend to longer times). LRA also showed a statistically significant higher use of contrast volume.

P1600 | BEDSIDE
Revascularisation did not improve short and medium term mortality in the elderly suffering from cardiogenic shock complicating an acute myocardial infarction: a meta-analysis
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Purpose: To test the hypothesis that revascularisation improves mortality in elderly patients with acute myocardial infarction (AMI) complicated by cardiogenic shock (CS).

Methods: A systematic review was performed identifying all randomised controlled trials about revascularisation improves mortality after AMI complicated by CS, when compared with medical therapy. The eligible trials were entered into this RevMan 5 software package. For dichotomous data, the risk ratio and 95% confidence intervals were calculated. We tested for heterogeneity with the chi-squared statistic, which was considered to be significant at p<0.10. Thus the results from the trials were pooled using the random effects model to allow generalisation of the results. 2 tests were used to assess the overall effect.

Results: Two eligible studies were found including a total of 111 patients (SHOCK and SMASH). 40 of 56 patients (71.4%) died within 30 days following revascularisation, compared with 35 of 55 (63.6%) who received medical therapy only [Risk ratio 1.10, 95% CI 0.69-1.75]. Figure 1. In the medium term, 42 of 56 (75%) died following revascularisation. This compares with 37 of 56 (67.2%) in the medically treated group. [Risk ratio 1.09, 95% CI 0.68-1.76]. In SHOCK trial, there was published data in patients aged ≥75, whereas in SMASH trial, we were only able to obtain data on patients aged 65-74. But even taking into account this younger cohort in SMASH trial, revascularisation did not appear to improve mortality. Definition of medium term differs slightly between the trials as we were only able to obtain 6-month mortality data in the SHOCK trial, and mortality up to 1 year in the SMASH trial.

Conclusions: Revascularisation did not improve mortality in the elderly suffering from CS complicating an AMI.

P1601 | BEDSIDE
Statin dosage and major adverse cardiovascular events after coronary artery bypass surgery
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Aim: Evaluation of MACE incidence, inflammation and endothelium injury markers under the postprocedural statin administration in different doses.

Material and methods: 88 patients exposed to PCI have been randomized in 2 groups to statin postprocedural administering dose: 1- simvastatin 80 mg/day during 1 month following by 20 mg/day during 11 months; 2- simvastatin 20 mg/day during 12 months. Incidence of MACE (myocardial infarction, stroke, unstable angina, in-stent restenosis and in-stent thrombosis) has been evaluated upon of 1 year surveillance. The circulating markers of inflammation and endothelium injury (hs-CRP, TNF-alpha, IL-6, NO and PLA2) were determined using ELISA and PLAG-Test preprocedurally and after PCI: 72 hours, 1, 3, 6 and 12 months.

Results: In I-st group the MACE incidence per one year was significantly lower compared to II-nd: 27.27% (12 pts) vs 38.64% (17 pts). Notable, that in I-st group no cases of in-stent restenosis were established. In the period of 72 hours after PCI has been established a significant rise of hs-CRP, TNF-alpha, IL-6, and PLA2 in both groups while the NO plasma concentration decreased. However, even in this short period the markers of I-st group shown an attenuated inflammatory response: hs-CRP (8.66±0.24 vs 7.73±0.29 g/L), TNF-alpha (6.52±0.28 vs 7.22±0.27 g/L), IL-6 (5.46±0.12 vs 6.53±0.18 g/L; p<0.05), PLA2 (341±21 vs 429±12 mm/ml; p<0.05), NO (58.85±2.8 vs 49.25±2.8 microm/L). At the period of 1 month after PCI the markers improved in both groups, but more evident in I-st, and due to this reason [7], [8]. In II-nd group, especially PLA2 level (238±16 vs 349±22 mm/ml; p<0.01). At distance of 3 months the markers have achieved preprocedural level only in I-st group, and after 6 months in II-nd group too. Remarkably, that during period 6-12 months the marker re-dressing dynamics was more rigid in II-nd group leading after 1 year to a conspicuous discrepancy (i.e II) of hs-CRP (3.17±0.12 vs 4.85±0.16 g/L; p<0.01) and TNF-alpha (4.11±0.23 vs 5.32±0.25 mm/ml; p<0.01).

Conclusions: (1) Postprocedural statin administration in high (aggressive) dose, 80 mg/day during 1 month, had a beneficial action on MACE evolution after PCI, reducing their incidence upon 1 year surveillance compared to statin dosage 20 mg/day from 38.64 to 27.27%. (2) High dose statin administration led to a more attenuated inflammatory response and endothelial injury after PCI confirmed by dynamics of postprocedural circulating levels of hs-CRP, TNF-alpha, IL-6, NO and PLA2.

CARDIOGENIC SHOCK, MECHANICAL SUPPORT AND CARDIAC SURGERY

P1603 | BEDSIDE
Extracorporeal life support in patients with refractory in-hospital cardiac arrest improves short-term and long-term survival
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Background: Cardiopulmonary resuscitation (CPR) is associated with low suc-
cess rates and variable survival outcome. Extracorporeal life support as an adjunct to CPR (ECPR) has shown encouraging survival rates in patients with refractory in-hospital cardiac arrest (IHCA). However, there is little information about the benefit of the procedure compared with conventional CPR (CCPR). The aim of this study was to compare the survival of patients receiving CCPR to that of patients with ECPR.

Methods: A total of 272 patients with witnessed IHCA of cardiac origin who had undergone CCPR and 52 patients with ECPR were included in this retrospective, propensity score-adjusted (1:1 matched), single-centre cohort study. All data were taken from hospital records. Routine laboratory parameters were measured at the time of admission and immediately after CPR and during post-IHCA care using standardised methods. The main endpoints were survival at 30 days, long-term survival, and neurological outcome defined by the Cerebral Performance Categories (CPC) score.

Results: The median follow-up duration after hospital discharge was 1136 days (IQR 823-1416). Unmatched patients with CCPR showed a tendency for better long-term survival over ECPR (37.5% vs. 23.1%; p=0.15). In the unmatched groups patients with ECPR had significantly higher initial APACHE II scores (20 (IQR 17.8-22.0) vs. 16 (IQR 12.5-19.0); p=0.003), increased dosage of norepinephrine (0.17 mcg/kg/min (IQR 0.06-0.65) vs. 0.09 mcg/kg/min (IQR 0.04-0.17); p=0.003), and significantly elevated levels of creatine kinase (CK) (431 UI (IQR 246-1271) vs. 143 UI (IQR 86-426); p<0.0001), CK-MB (57 UI (IQR 32-154) vs. 41 UI (IQR 25-84); p<0.0001), creatinine (1.7 mg/dl (IQR 1.03-3.0) vs. 1.16 mg/dl (IQR 0.88-1.67); p=0.041), and lactate (3.6 mmol/l (IQR 1.59-8.4) vs. 2.02 mmol/l (IQR 1.24-4.02); p=0.02) before CPR compared to CCPR. After equalizing these parameters significant differences were observed in short-term and long-term survival during CPR over CCPR (27% vs. 17%; p=0.01 (short-term) and 23.1% vs. 11.5%; p=0.008 (long-term); hazard ratio [HR] 0.59 95% CI 0.39-0.91; p=0.02). There was no significant difference in CPC score between the groups (CCPR 1 (IQR 1.0-3.0) vs. 1.5 (IQR 1.0-3.0); p=0.40). Conclusion: In our cohort study ECPR had short-term and long-term survival benefits over CCPR in patients with witnessed-in-hospital cardiac arrest of cardiac origin.

P1604 | BENCH
Mechanically unloading the left ventricle and delaying coronary reperfusion limits myocardial infarct size
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Contemporary management of an acute myocardial infarction (AMI) focuses on restoring oxygen supply to limit myocardial damage. Recent data shows that more rapid coronary reperfusion fails to improve survival after AMI. The Impella CP axial-flow pump (Abiomed Inc) is designed to reduce left ventricular stroke work (LVSW). We tested the hypothesis that first reducing myocardial work and delaying coronary reperfusion improves myocardial salvage.

Methods: Left anterior descending artery (LAD) occlusion was induced by angioplasty for 90 minutes in 500g male Yorkshire swine (n=5/group). LV pressure-volume loop analysis was performed in all animals. In Group 1, the LAD was reperfused for 120 minutes. In Group 2, after 90 minutes of ischemia the Impella CP device was activated and the LAD left occluded for an additional 60 minutes (150 minutes of LAD occlusion total), followed by 120 minutes of reperfusion. The Impella CP was active throughout reperfusion.

Results: Compared to Group 1, Group 2 had reduced LVSW (1223±337 vs 504±389, p=0.03), LV end-diastolic volume (202±15 vs 125±36, p<0.01), and LV end-diastolic pressure (17±4 vs 8±4, p=0.01) after reperfusion (Fig. 1A). After protocol completion, hearts were perfused with Evans blue dye to calculate the area at risk (AAR), then counterstained with triphenyltetrazolium chloride to quantify infarct size. Compared to Group 1, the percent myocardial infarct size compared to the AAR was reduced in Group 2 (73±13% vs 42±15% p=0.02; Fig. 1B).

Conclusion: In contrast to the paradigm of primary PCI, we report the potential benefit of primarily unloading the heart with an axial-flow catheter and delaying coronary reperfusion to salvage myocardium in AMI. This is the first report to examine the potential utility of the Impella CP in myocardial salvage.

P1605 | BEDSIDE
Hospital volume has significant impact on mortality with cardiogenic shock patients who are in need of mechanical circulatory support
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Purpose: Despite the technical advances in cardiology, cardiogenic shock as a complication of acute myocardial infarction (AMI) remains a difficult challenge. Therapeutic guideline of mechanical circulatory support has not yet been established; initiating and terminating mechanical support is solely based on experiences of each individual hospital. However, data are lacking on the association between hospital experience and outcomes of mechanical support. We therefore investigated the relationship between hospital volume and mortality of mechanical support using a national inpatient database.

Methods: Using the Japanese Diagnosis Procedure Combination Database combination between 2007 and 2013, we extracted AMI patients who underwent mechanical circulatory support (ventricular assist device, extracorporeal membrane oxygenation, and intra-aortic balloon counterpulsation). We performed multilevel logistic regression analyses fitted with generalized estimating equations because the data were clustered within hospital. Hospital volumes were categorized into tertiles (H1 - 11 per year, medium; H2 - 21-22; and high-volume, >52). The outcome was 30-day all-cause mortality. Predictor variables were age, gender, smoking habit, Killip class at admission, ventilator support, type of mechanical circulatory support, prior history of stroke, location of infarction (anterior or non-anterior), prior heart failure, global rate of hospital, academic hospital or not, and hospital type.

Results: Of the 159337 AMI patients, 23679 underwent mechanical support. 4831 patients (20.4%) died within 30 days after admission. Compared to the low-volume group, the odds ratios of 30-day mortality for medium- and high-volume groups were 0.68 [95% confidence interval, 0.60-0.78] and 0.80 [0.71-0.91], respectively. Higher age, female gender, higher Killip class, Patients with ventilator support, those with extracorporeal membrane oxygenation, those on dialysis and those hospitalized at non-academic hospitals were likely to die.

Conclusions: Hospital volume had a significant impact on mortality of AMI patients who were in need of mechanical supports. Policymakers need to consider hospital experiences when developing strategies to improve access to primary angioplasty of AMI patients.
**P1607 | BEDSIDE**

Impact of a mechanical circulatory support program in the survival of patients with cardiogenic shock due to an acute myocardial infarction that underwent primary angioplasty


**Purpose:** Primary angioplasty is the best reperfusion therapy for ST elevation myocardial infarction. Patients in cardiogenic shock benefit from mechanical reperfusion, but their mortality remains high even after the placement of an intra-aortic balloon. There is no clear information regarding whether an ongoing Mechanical Circulatory Circulation Support Program (MCSPP) might improve the long-term outcome of these patients. We have analyzed the clinical impact of a MCSPP in this setting.

**Methods:** We have compared the in-hospital and 1 year survival of patients in cardiogenic shock in the setting of a primary angioplasty with inserted intra-aortic balloon in two different periods of time. The first period before and the second after the implantation in our hospital of a MCSPP. This program included the incorporation of a specially trained staff and the availability of the extracorporeal membrane oxygenation device (ECMO) and the left ventricular or biventricular assist devices (LVAD, bivAD). Following inclusion criteria required: STEMI, cardiogenic shock by clinical and hemodynamic data, primary angioplasty and intra-aortic balloon inserted. Patients with cardiogenic shock due to mechanical complications were excluded.

**Results:** We included 42 consecutive patients in the first period “pre-MCSP” and 56 in the second period “post-MCSP”. Clinical baseline characteristics were very similar in both groups except for a wider use of drug eluting stents in the second period (19% vs 40%; p=0.03). In the “post-MCSP” group 9 (16%) patients needed an ECMO and 8 (14.3%) a ventricular assist device. Six patients were included in the cardiac transplant list in the “pre-MCSP” group and four in the “post-MCSP” group. Three patients in each group finally underwent a cardiac transplant. In-hospital survival was 49.9% in the “pre-MCSP” group compared to 67.2% in the “post-MCSP” group (p=0.03). The 12 months survival was 39.8% in the “pre-MCSP” group vs. 59.5% in the “post-MCSP” group (p=0.03). The multivariate logistic regression revealed a higher risk of death in the “pre-MCSP” period (HR 2.5, CI 95% 1.04-7.5; p=0.03).

**Conclusions:** The implementation of a mechanical circulatory support program improves significantly the prognosis of patients in cardiogenic shock in the setting of a primary angioplasty.

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**P1608 | BEDSIDE**

Effect of extracorporeal membrane oxygenation (ECMO) therapy for acute respiratory failure increases platelet-monocyte and platelet-neutrophil complex formation within 24 hours after initiation of therapy

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**Background:** Anticoagulation management in ECMO therapy is challenging since bleeding complications are known to be associated with this therapy. We hypothesized that platelet reactivity assessed by platelet-monocyte (PMC) and platelet-neutrophil complex (PNC) formation is a read-out and could serve as a potential therapeutic target to decrease bleeding events.

**Methods:** Patients with acute respiratory failure requiring extracorporeal membrane oxygenation were subsequently included in a single center prospective study. Patients on treatment with antiplatelet drugs were excluded. Blood samples collected immediately before initiation of extracorporeal circulation and at 24 and 48 hours were used to assess PMC- and PNC-formation by flow cytometry via a CD41/CD45/CD14 or CD15 gating strategy. Platelet activation was assessed by P-selectin expression and binding of the GPIIb/IIIa activation-specific antibody PAC-1.

**Results:** We included 12 patients (17% female, 83% male) with a mean age of 59±12 years and a mean time with extracorporeal circulation of 4.3 days. On-therapy mortality was 33%, bleeding events occurred in 38% of the cases. A significant increase in ADP-induced PMC-formation was observed after 24 hours on extracorporeal circulation from a mean of 6.1% to 43.6% (p=0.049). ADP-induced PNC formation was also significantly increased at 24 hours from a mean of 4.9% to 26.8% (p=0.048). Leukocyte count was unaffected, platelet count decreased over time, PAC-1 binding to the platelets increased from 0–72 hours.

**Conclusion:** Platelet reactivity is significantly increased upon initiation of extracorporeal circulation leading to increased platelet reactivity and platelet-leukocyte complex formation. Therapeutic approaches to reduce platelet reactivity could therefore offer a novel concept to prevent bleeding complications associated with ECMO therapy.

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**P1609 | BEDSIDE**

Impact of models for end-stage liver disease score on outcome in patients with percutaneous extracorporeal membrane oxygenation who are scheduled to receive ventricular assist device implantation as ‘bridge to bridge’ therapy


**Purpose:** Models for end-stage liver disease (MELD) score, an objective index for assessing end organ function such as liver and kidney, has been recently found to be useful in predicting the prognosis of patients with heart failure. In this study, we tried to elucidate the prognostic values of MELD score in patients with severe hemodynamic instability supported by percutaneous extracorporeal membrane oxygenation (p-ECMO) who were scheduled to receive ventricular assist device (VAD) implantation as “bridge to bridge” therapy.

**Methods:** We retrospectively reviewed consecutive 131 patients who underwent VAD implantation at the National Cerebral and Cardiovascular Center from April 2001 to December 2013. Patients who received p-ECMO insertion prior to VAD implantation were analyzed in more detail from there clinical characteristics and they were stratified according to their MELD score that were calculated just before their VAD implantation.

**Results:** In the study period, 30 patients (mean age 32.2±11.1 years, 20 males) received p-ECMO insertion prior to VAD implantation. These 30 patients underwent paracorporeal VAD implantation and demonstrated significantly lower survival rates during their VAD support period compared to those without p-ECMO insertion prior to VAD implantation (2-years survival rate, 66.2% vs 82.7% respectively, p=0.015, log-rank test). Of these 30 patients, 8 patients were successfully bridged to heart transplantation, whereas 13 patients died. Five patients were successfully weaned from VAD and 4 patients have been still supported by VAD at the end of study period. Univariate cox proportional hazard model demonstrated that MELD score significantly predict poor prognosis during their VAD support period (hazard ratio, 1.08; 95% confidence interval, 1.02-1.15; p=0.0093). Kaplan-Meier analysis revealed that a MELD score 16 or higher (high MELD group) was a strong predictor of mortality during their VAD support period (p=0.0015, log-rank test). Clinical characteristics prior to VAD implantation were compared between patients with MELD score less than 18 and those in high MELD group and diastolic dimension of left ventricle was significantly small in patients with high MELD group.

**Conclusions:** Preoperative p-ECMO support itself was the risk factor for following VAD implantation. However, end organ function calculated by MELD score have potential to predict the prognosis in patients with p-ECMO who are scheduled to receive VAD implantation.

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**P1610 | BEDSIDE**

Effect of intra-aortic balloon counterpulsation on short-term survival in cardiogenic shock


**Purpose:** Although current guidelines recommend intraaortic balloon counterpulsation (IABP) treatment in cardiogenic shock complicating acute myocardial infarction, a recent controlled randomized trial (IABP-SHOCK II) detected no survival benefit among patients treated with IABP. However, subgroup analysis revealed a near-significant interaction between IABP and age.

**Methods:** We extracted data for all consecutive patients with cardiogenic shock undergoing percutaneous coronary intervention (PCI) between 2004 and 2013 from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) for five hospitals in western Sweden. Logistic regression adjusted for propensity score were used to compare the groups in regard to 30-days mortality. Analyses were performed with complete data and using multiple imputation methods. Background characteristics and procedural data were used to calculate propensity score.
Purpose: The ability to assess risk of mortality in patients undergoing insertion of a Left Ventricular Assist Device (LVAD) is important in ensuring appropriate patient selection. This study sought to assess the validity of using the Heartmate II Risk Score (HMRS) in the Heartware LVAD population.

Methods: We retrospectively reviewed all patients (n=75) undergoing insertion of a Heartware LVAD at our centre from 2007 onwards. Pre-operative measurement (age, albumin, creatinine and INR) were collected, and risk scores were calculated using the HMRS calculation. The endpoints for the study were 90-day mortality, 1-year mortality, and 1-year transplant free survival.

Results: The ability to assess risk of mortality in patients undergoing insertion of an LVAD is important in ensuring appropriate patient selection. The study validated the use of the HMRS in the Heartware LVAD population.

Conclusions: In this small cohort, the Heartmate II Risk score is not predictive of 90-day or 1-year mortality in this Heartware population, although overall the mortality rates are significantly lower in this study population than in the initial HMRS derivation cohort.

P1612 | BEDSIDE
Risk of bleeding after coronary artery bypass grafting according to body mass index: A nationwide cohort study
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Purpose: The obesity paradox has been proposed to influence outcome after Coronary Artery Bypass Grafting (CABG). Previous studies have found a J-shaped relationship between risk of both bleedings and adverse cardiovascular outcomes and Body Mass Index (BMI). We conducted a study to investigate bleeding risk among CABG patients according to BMI in a nationwide cohort.

Methods: We included CABG patients > 30 years admitted 2006-2011. Patients were followed for 1 year. Information on comorbidity and concomitant medication was identified by individual-level linkage of administrative registers. Patients were divided into weight classes according to WHO criteria. Hazard ratios (HRs) on 1) Fatal or non-fatal bleedings, requiring hospitalization and 2) Recurrent myocardial infarction, ischemic stroke or cardiovascular was assessed by Cox proportional Hazard Model, adjusted for age, gender, inclusion year, comorbidity, medication, previous bleeding, alcoholism & Euroscore, with normal weight (18.5–BMI < 25) as reference.

Results: A total of 9542 patients (mean age 68 SD 12, 79% male) were included. Underweight patients (BMI < 18.5) and Obese Class III patients (BMI > 40) had the most bleedings within weight class (6.7% and 7.1%, respectively). Patients in Obese Class I (BMI < 30) had significantly less risk of bleeding (HR: 0.7, 95%CI: 0.6-0.9, P=0.027). Overweight (25–BMI < 30) and Obese Class I patients had significantly less risk of cardiovascular events (HR: 0.8, 95%CI: 0.6-0.9, P=0.016 and HR: 0.7, 95%CI: 0.5-0.9, P=0.004, respectively).

Conclusions: Obese Class I patients were less prone to bleed and Obese Class I and overweight patients had lesser risk of cardiovascular events after CABG. Our results concur with previous findings on the obesity paradox.

P1613 | BEDSIDE
Arterial closure devices in minimally invasive heart surgery
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Background: Arterial closure devices (ACDs) were introduced to replace standard compression at the puncture site following percutaneous intervention. They allow percutaneous placement of larger cannulas. To date there is no published evidence on the use of such devices during minimally invasive cardiac surgery (MICS), where cannulation through the femoral vessels is necessary. We report our results comparing the use of ACDs with conventional surgical closure of vascular access on patients undergoing MICS.

Methods: We analyzed retrospectively 167 consecutive patients, who underwent minimally invasive cardiac surgery with groin cannulation between 9/2010 and 4/2013. Operative procedures included mitral valve repair/replacement, tricuspid valve repair/replacement, ASD closures and myxoma excisions. Of these, 89 (53%) had closure of vascular access through the use of ACD. Patients were included except for a higher incidence of endocarditis in the ACD group (10 vs 2, p<0.05). There were no significant differences between preoperative characteristics of both groups. There was also no significant difference between groups with regard to procedure characteristics including cardiopulmonary bypass duration (133±41min) or cardioplegia size used (19±19). Overall 30-day mortality was 2.39% and not different between groups. Complications at the cannulation site consisted of fistulae (n=2), wound infections (n=2) and hematoma (n=1). All of them occurred in the conventional group. There was no difference in length of hospital stay or days-to-mobilization.

Conclusions: Our results indicate a benefit for ACDs in MICS, although the number of cases was low in both groups. The results justify the conduct of a prospective randomized trial.

P1614 | BEDSIDE
Incidence and outcome of surgical procedures after coronary artery bypass grafting compared with those after percutaneous coronary intervention
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Background: Non-cardiac surgery after percutaneous coronary intervention (PCI) has been reported to be carrying high risk for both ischemic and bleeding complications. However, there has been no report comparing the incidence and outcomes of surgical procedures after coronary artery bypass grafting (CABG) with those after PCI.

Methods and results: Among 14383 patients undergoing first coronary revascularization (PCI: N=12207, and CABG: N=2176) enrolled in the CREDO-Kyoto registry cohort-2, surgical procedures were performed more frequently after CABG (N=560) than after PCI (N=2398) (cumulative incidence at 3-year: 27% versus 22%, P<0.0001), particularly within 6-month of coronary revascularization. The risk for the primary ischemic outcome measure (death/myocardial infarction) at 30-day post-surgical procedures was not significantly different between the CABG and PCI groups (cumulative incidence: 3.1% versus 3.2%, P=0.9, and adjusted hazard ratio [HR]: 0.97, 95% confidence interval [CI]: 0.47-1.89, P=0.9). The risk for the primary bleeding outcome measure (moderate or severe bleeding by GUSTO classification) was lower in the CABG groups than in the PCI group (cumulative incidence: 1.3% versus 2.6%, P=0.07, and HR: 0.36, 95%CI: 0.12-0.87, P=0.02). There were no interactions between the timing of surgery and the types of coronary revascularization modalities (CABG/PCI) for both the ischemic and bleeding outcome measures.

Conclusions: Surgical procedures were performed significantly more frequently after CABG than after PCI, particularly within 6 months after coronary revascularization. Surgical procedures after CABG as compared with those after PCI were associated with similar risk for ischemic events and lower risk for bleeding events, regardless of the timing after coronary revascularization.
DISEASE OF THE AORTA AND MEDICAL THERAPY

P1616 | BEDSIDE
The incidence and risk factors of acute kidney injury in type A acute aortic dissection
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Purpose: Acute kidney injury (AKI) after cardiothoracic surgery for acute aortic dissection (AAD) is relatively common and increases mortality. However, there are few data on the incidence and risk factors of AKI in AAD patients, as well as the impact of AKI on in-hospital mortality. In the present study, we investigated the incidence and risk factors of AKI in AAD patients.

Methods: 416 consecutive patients diagnosed as AAD (Stanford classification type A) at our institute (a 320-bed, tertiary-level heart center) between October 2006 and March 2013 were analyzed retrospectively. AKI was defined by RIFLE criteria, which is based on serum creatinine or glomerular filtration rate. Multivariate logistic regression analysis was performed to evaluate the attributable risk of AKI on in-hospital mortality. Stepwise Cox proportional hazards analysis was also performed to identify independent predictors of AKI.

Results: Among the 416 patients, 392 patients (94.2%) received emergent surgical procedures, involving the ascending aorta (59.4%), aortic arch (38.0%), aortic valve (12.5%). The overall in-hospital mortality was 6.3%, and the incidence of AKI was 44.4%. The independent risk factors of AKI were coronary ostial involvement and longer cardiopulmonary bypass duration. In multivariate logistic regression analysis, AKI was significantly associated with in-hospital mortality (HR 4.56, p=0.007) after adjustment of other clinical factors including age, gender, obesity, hemodynamic instability, neurological deficit before operation, coronary ostial involvement and longer cardiopulmonary bypass duration. Kaplan-Meier analysis also showed that the in-hospital mortality was strongly correlated with the severity of AKI by RIFLE criteria.

Conclusions: Acute kidney injury was common in the patients with type A acute aortic dissection. Since it was a strong predictor of in-hospital mortality, AKI should be taken into consideration in the perioperative period.

P1617 | BEDSIDE
The impact of acute kidney injury on long-term prognosis of type A acute aortic dissection
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Purpose: Acute aortic dissection (AAD) is the most common catastrophic event affecting the aorta, and surgical treatment is an option for type A and complicated type B. It has been reported that acute kidney injury (AKI) is an independent outcome predictor in patients with cardiothoracic surgery. However, few data were reported about the impact of AKI on long-term prognosis in patients undergoing surgical treatment for AAD.

Methods: We examined 375 consecutive patients who underwent open surgery for Type A AAD between October 2007 and March 2013 at our hospital retrospectively. Cox regression analysis was performed to reveal the relationship between the risk of major adverse cardiac and cerebrovascular event after discharge (MACCE: death, non fatal MI, stroke) and peripertative AKI. AKI was defined by RIFLE criteria, which is based on serum creatinine or glomerular filtration rate.

Results: AKI is significantly associated with MACCE (P=0.007) and overall mortality (P=0.021). Kaplan-Meier analysis of patients in each grade of AKI during hospitalization (risk, injury, failure,Loss,EESRD, deceased) revealed well correlation with the long-term prognosis.

Conclusions: We suggest an association between the grade of acute kidney injury and MACCE and long-term mortality in patients undergoing open surgical therapy for Type A acute aortic dissection. Acute kidney injury in hospital can be a predictive indicator for prognosis of Type A acute aortic dissection from date of hospital discharge.

P1618 | BEDSIDE
Impact of development of localized dissection on clinical outcomes in acute phase of type B aortic syndromes
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Background: Aortic guidelines recommend a similar treatment in Type B aortic dissection (AD) and intramural haematoma (IMH) in patients with the same clinical risk. However, the differences in prognosis in a short-term follow-up depending on the morphological changes in the acute phase of each entity remain unknown.

Objectives: To compare morbidity and mortality of type B AD vs IMH with and without development of Localized Dissection (LD) in acute phase in short-term follow-up.

Methods: 171 patients, 86 (50%) IMH without LD (Fig. 1A), 5 (3%) IMH with LD (Fig. 1B) and 80 (47%) AD (Fig. 1C), were included prospectively in a clinical and imaging protocol. Aortic and overall mortality, surgical interventions and visceral ischaemia were collected to evaluate the clinical prognosis. LD was defined as a localized blood-filled pouch in the damaged aortic wall with a communicating orifice >3mm with periaortic haematoma associated.

Results: Patients with IMH and LD were older (p=0.001) and presented a higher basal maximum aortic diameter (MAD) at diagnosis (IMH vs AD: 55.6±12.7, IMH without LD: 41.5±8.3, AD: 41.1±8.8mm; p=0.02). During the hospitalization, IMH with LD cases showed a higher overall mortality (p<0.001), due to the higher aortic mortality (p<0.001), and a higher number of cases treated invasively (p<0.001). A multivariate logistic regression analysis, including age and MAD, indicated the development of LD as the only independent predictive factor of aortic mortality in type B acute aortic syndromes (AAS) (OR=17.5; CI 95%:3.4-93.4).

Conclusions: Development of LD in Type B IMH implied a higher risk of aortic complications in short-term follow-up than other AAS, independently of MAD and age. More aggressive management in this subgroup of patients is advisable if they share the same clinical conditions.

P1619 | BENCH
Prediction of cardiac and vascular events in systemic sclerosis: input from Endothelin-1 type A receptor antibodies
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Background: Cardiac and peripheral microvascular alterations are key features of systemic sclerosis (SSc). We have previously reported that angiogenic markers can predict the cardiovascular outcomes in SSc. In parallel, a cross-sectional study reported an association between severe cardiovascular complications and functional antibodies against angiotensin II type 1 receptor (AT1R) and Endothelin-1 type A receptor (ETAR).

Objectives: Our aim was to investigate the respective merit of all these markers in a prospective cohort.

Methods: Serum levels of anti-AT1R and anti-ETAR autoantibodies, placenta growth factor (PIGF) and soluble vascular adhesion molecule (sVCAM) were measured with sandwich ELISA in a prospective cohort of 75 SSC patients. Circulating endothelial progenitor cells (EPCs) were quantified in peripheral blood by flow cytometry after cell sorting. The occurrence of at least one cardiac/vascular event was assessed during a planned 3-year follow-up by a composite index defined by the occurrence of at least one of the following event: a) one or more new ischemic digital ulcer (DU); b) pre-capillary pulmonary hypertension (PH) confirmed by right heart catheterization; c) left ventricular (LV) dysfunction, defined by a LV ejection fraction (EF) <50%; d) scleroderma renal crisis (SRC).

Results: The mean age of SSc patients (84 women) was 55±12 year old and the mean disease duration was 9.6±8 years at baseline. Twenty-eight patients developed at least one cardiac/vascular event (DU in 18, PH in 5, LV dysfunction in 4 and SRC in a single patient). By univariate analysis, high baseline serum levels of anti-ETAR were predictive of the occurrence of cardiac/vascular events (p=0.002), together with low EPC counts (p=0.003) and increased levels of PIGF (p=0.0005) and sVCAM (p=0.009). No predictive value of anti-AT1R antibodies was identified. Multivariate analysis confirmed high serum levels of anti-ETAR antibodies (hazard ratio, HR: 3.71, 95%CI 1.44-9.52, p=0.03) and PIGF (HR: 5.22, 95%CI
Polymorphism -8202 A/G (rs11697325) of MMP-9 gene (p=0.02). There was tendency to increase of borderline statistical significance in the distribution of alleles, being C allele more had family history of sudden death (SD). The -735 C/T polymorphism (rs2285053) weren't differences in genotypes between pts with bicuspid aortic valve (BAV) and Sweden; 2 Stanford University, Stanford, United States of America

P1621 | BEDSIDE
Association of matrix metalloproteinase 2 and 9 genes single nucleotide polymorphisms with matrix metalloproteinase activity and thoracic aortic aneurysm development

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Objectives: Thoracic aortic aneurysm (TAA) is genetically heterogeneous disorder, characterized by extracellular matrix abnormalities. Matrix metalloproteinases (MMP) 2 and 9 play important role in aortic root dilatation. Purpose of this study was to identify genetic variants of single nucleotide polymorphisms (SNP) of MMP-2 and -9 genes associated with TAA.

Methods: Genomic DNA was isolated from blood of 251 pts with TAA (mean age 55.5±10.3, m/f ratio 2:8.1) and 227 controls (mean age 56.8±9.4, m/f ratio 1:8.1). Polymorphism -8202 A/G (rs11697325) of MMP-9 and -735 C/T (rs2285053) analyzed using real time polymerase chain reaction. The activity and relative abundance of MMP-9 gene was assessed in aortic tissue samples from 27 TAA pts and 9 controls by quantitative immunoblotting techniques and substrate-specific zymographic analysis.

Results: Maximum aortic diameter was 54.5±10.3 mm in pts with TAA. There weren't differences in genotypes between pts with bicuspid aortic valve (BAV) and controls. MMP-2,9 gene was significantly associated with SD (p=0.016). The revealed a borderline significant difference in the distribution of alleles, being C allele more frequent in patients with TAA. Aortic diameter was associated only with -8202 A/G (rs11697325) of MMP-9 gene (p=0.02). There was tendency to increase of level of MMP-9 in patients with genotype AA of MMP-9 gene polymorphism -8202 A/G.

Clinical characteristic of the group

TAA (M±SD) Control (M±SD)
Age, years 55.5±10.3 56.8±9.4
Maximum aortic diameter, mm 54.5±10.3 34.5±3.7
M/F ratio 2:8.1 1:8.1

Conclusion: Specific genotypes of MMP-2 and -9 genes polymorphisms could be in part responsible for TAA development. Some genotypes of MMP-9 SNP are associated with greater dilatation of aorta. Genotyping of MMP-2 and -9 could be useful for estimating of non-modifiable risk factors in patients with TAA and also for relatives screening. Higher incidence of sudden death at a low frequency of family aneurysm can be explained by low detection of TAA.

P1621 | BENCH
Diagnostic and prognostic biomarker potential of miR-24 in abdominal aortic aneurysm disease and rupture

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Objectives: MicroRNAs (miRNAs) have been identified as crucial posttranscriptional inhibitors of gene expression in response to stress and injury in cardiovascular disease (CVD) by regulating the expression levels of their target mRNAs. Lately, they have received much attention regarding their suitability and feasibility as biomarkers for aortic stent grafts (bio stent grafts) using in-body tissue architecture (diameter: 8.6 mm, length: 40 mm) into self-expanding nitinol stents (diameter: 9.0 mm, length: 35 mm). The miRs (n=6) were embedded into subcutaneous space of a beagle (n=3 beagles for 4 weeks. Upon trimming excessive tissues around the mold after harvesting and removing each rod, the stents completely covered with autologous tissue membranes were obtained as BSGs (Photo A). Of 6 stent grafts, 3 implants were implanted into abdominal aorta of beagles via the femoral approach (in the PPE model), as well as aortic rupture (in the AngII model) by expressing the expression of the gene ctninasa3-like (Ch311), which regulates macrophage survival and cytokine release (from invading peripheral macrophages) in expanding murine AAs. Finally, the expression of miR-24 was significantly and substantially different in plasma samples from human patients with acutely ruptured AAs (n=7) compared to patients with non-ruptured AAAs (abdominal aortic diameter between 55-78 mm; n=7) undergoing surgical repair, as well as un-diseased controls (n=7).

We explored the diagnostic and prognostic biomarker potential of miRNAs released into circulation during aortic endoleak propagation, and ultimately rupture of AAAs in mice and humans. The identification of miR-24 potentially offers great prognostic value to determine which patients present with increased risk of rapid AAA expansion and subsequent rupture.

P1622 | BEDSIDE
Neutrophil-lymphocyte ratio in acute aortic dissection

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Purpose: Acute aortic dissection (AAD) is a life-threatening disease. Neutrophil-lymphocyte ratio (NLR) is an index of systemic inflammation associated with increased cardiovascular mortality. We investigated NLR in a group of patients with AAD compared with patients with chronic aneurysms and a control group of healthy volunteers.

Methods: We evaluated pre-operative NLR, white cell blood count (WBC), platelets count (PLTs) C-reactive protein (CRP), D-dimer and cardiac enzymes in 120 consecutive patients with AAD admitted for emergency surgery (63±14 years old, 89 men), 121 consecutive patients with chronic aneurysms of the ascending aorta admitted for elective repair (63±11 years old, 90 men) and 121 healthy controls (63±14 years old, 90 men).

Results: Levels of NLR, PLTs, WBC, CRP, D-dimer, creatine kinase (CKP), creatine kinase-MB (CK-MB) and troponin I (Tn-I) are expressed in median (interquartile range 25th-75th percentile) and are presented in Table. Patients with AAD had significantly higher elevated NLR, compared to chronic aneurysms and normal controls (p<0.001). Significant associations were observed between NLR and D-dimer (r=0.31, p=0.003), CKP (r=0.23, p=0.013) and CK-MB (r=0.26, p=0.005) in patients with AAD.

Table 1. Levels of neutrophil-lymphocyte ratio, WBC, PLTs, CRP, D-dimer and cardiac enzymes in acute aortic dissection, uncomplicated chronic aneurysms and normal controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Aortic dissection</th>
<th>Chronic aneurysms</th>
<th>Controls</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil-lymphocyte ratio, n=120</td>
<td>10.1 (5.9, 14.3)</td>
<td>2.2 (1.7, 2.9)</td>
<td>2 (1.4, 3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>White cell blood count, K/uL</td>
<td>12200 (14800, 21500)</td>
<td>8700 (19000, 25900)</td>
<td>7300</td>
<td>0.001</td>
</tr>
<tr>
<td>Platelets count, K/uL</td>
<td>100000 (16000)</td>
<td>6400 (8600)</td>
<td>6100 (8700)</td>
<td>0.001</td>
</tr>
<tr>
<td>C-reactive protein, mg/l</td>
<td>8.6 (3.19, 18.7)</td>
<td>2.3 (1.2, 5.8)</td>
<td>2.1 (1.1, 5.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>D-dimer, ng/ml</td>
<td>5433.5</td>
<td>456</td>
<td>234.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Troponin I, ng/ml</td>
<td>114 (65, 277)</td>
<td>161 (44, 232)</td>
<td>73 (53, 107)</td>
<td>0.001</td>
</tr>
<tr>
<td>Creatine kinase-MB, ng/ml</td>
<td>1.9 (0.3, 4.8)</td>
<td>0.7 (0.3, 1.1)</td>
<td>0.7 (0.3, 1.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: In addition to leucocytosis, pre-operative NLR ratio is higher in patients with AAD compared to chronic uncomplicated aneurysms and normal subjects.

P1623 | BENCH
Development and implantation of tissue engineered self-expandable aortic stent grafts (bio stent grafts) using in-body tissue architecture technology in beagles

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Purpose: Stent grafts which can assimilate to native aorta are desirable for avoiding endoleaks and migration. We have developed autologous prosthetic materials with excellent mechanical and biocompatibility using “in-body tissue architecture” technology, which is a practical approach of regenerative medicine based on the tissue encapsulation phenomenon. Using the technology, we firstly developed novel stent grafts covered with only autologous tissue (bio stent grafts: BSG). Their in vivo preparation method and early adaptation to aorta in a beagle model will be presented.

Methods: Preparation molds for BSG were assembled by insertion of acrylic rods (diameter: 8.6 mm, length: 40 mm) into self-expanding nitinol stents (diameter: 9.0 mm, length: 35 mm). The molds (n=6) were embedded into subcutaneous space of a beagle (n=3 beagles for 4 weeks. Upon trimming excessive tissues around the molds after harvesting and removing each rod, the stents completely covered with autologous tissue membranes were obtained as BSGs (Photo A). Of 6 stent grafts, 3 implants were implanted into abdominal aorta of beagles via the femoral...
Patients with high score (n=31) compared with subjects with low score had in-group (low score) had normal IMT and absence of plaques at all four arteries.

Smoking status. Receiver operating curve analysis showed that PWV these two groups did not differ regarding blood pressure, metabolic profile and PWV than was femoral IMT (Fig. 1C, D). On the contrary carotid IMT was more strongly related to aortic entire population, femoral IMT was more strongly related to PSV than was carotid IMT (Fig. 1A, B). Our study shows that aortic PWV and penile PSV correlate significantly with aortic PWV and penile PSV correlate significantly with carotid and femoral atherosclerotic burden. These data suggest a close interrelationship between ED progression, increased aortic stiffness and total atherosclerotic burden.

Conclusions: The BSGs prepared by short-term embedding of the molds into subcutaneous layer were completely fused with native aorta in short-term implantation, which may avoid endoleaks and migration.

P1624 | BEDSIDE
Association of total atherosclerotic burden with aortic stiffness and progression of penile vascular disease
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Purpose: We investigated whether total atherosclerotic burden is related to aortic stiffness and penile vascular disease severity by using a classification that incorporates intima media thickness (IMT) and plaques from both the carotid and femoral arteries.

Methods: Sixty-five patients (58±12 y/o) underwent a dynamic penile Doppler ultrasound. Penile peak systolic velocity (PSV) shows the greatest flow velocity detectable in an artery throughout the systole. Ultrasoundographic measurements of IMT and plaques in the carotid and femoral arteries were evaluated and a previously described ultrasound-based morphological classification was used. Aortic stiffness was evaluated with carotid-femoral pulse wave velocity (PWV).

Results: Patients were classified into two groups: One group (high score) had increased IMT (> 1.0 mm) and/or plaque in either of the four arteries and the other group (low score) had normal IMT and absence of plaques at all four arteries. Patients with high score (n=31) compared with subjects with low score had increased age-adjusted PWV (P < 0.001) and decreased PSV (P < 0.006), whereas these two groups did not differ regarding blood pressure, metabolic profile, smoking status. Receiver operating curve analysis showed that PWV > 8.6 m/s and PSV < 30 cm/s were the optimal cutoff values to predict a high score. In the entire population, femoral IMT was more strongly related to PSV than was carotid IMT (Fig. 1A, B).

Conclusion: Patients with aortic disease compared to those without aortic disease had significantly higher long-term risk for cardiovascular events. Statins therapy in patients with aortic disease was associated with lower risk for cardiovascular events with an event size similar to that observed in patients without aortic disease.
1216 (10.8%) were treated with ACEIs and 430 (3.8%) received ARBs at baseline. Crude incidence rates of death from AAA per 100 patient-years were 3.7, 3.9 and 3.2 for treatment with ACEIs/ARBs (ACEIs or ARBs as a group), ACEIs, and ARBs, respectively. Hazard ratios (HRs) for death from AAA were 0.73 (95% CI 0.60-0.99, P=0.043) for those receiving ACEIs, and 0.77 (95% CI 0.60-0.99, P=0.043) for those receiving ARBs, respectively. The difference in HRs between ACEIs and ARBs was not significant (P=0.706). Results for all outcomes are shown in the figure.

Hazard ratios for all study endpoints.

Conclusions: Treatment with ACEIs or ARBs is associated with a comparable reduction of mortality in patients with AAA.

P1629 | BEDSIDE

Pre-procedural risk factors for contrast-induced nephropathy in patients undergoing primary percutaneous coronary intervention

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Purpose: Few Risk Scores for contrast induced nephropathy (CIN) in patients undergoing primary percutaneous coronary intervention (PCI) are available in the literature. So far, post-procedural risk factors of CIN have been suggested, but they cannot be used for pre-procedural risk evaluation since the scores include variables which are not yet known, such as amount of contrast medium and use of IABP. The aim of this study was to define pre-procedural risk factors of CIN in a single centre homogeneous population.

Methods: We prospectively enrolled consecutive STEMI patients undergoing pPCI in our centre in 2005-2012 (n=1538 after exclusion of 15 patients without creatinine values after pPCI). CIN was defined as an increase in creatinine >0.5mg/dl in the first 72 hours; chronic kidney disease (CKD) was defined as an estimated GFR <60 ml/min. Independent predictors of CIN were evaluated with a multivariable logistic regression model.

Results: CIN occurred in 85 patients (5.5%). Patients with CIN were older, had more frequently anterior MI, a higher Killip class, a higher baseline creatinine, a TIMI flow <3 after PCI, a higher CK peak and a lower in-hospital left ventricular ejection fraction (all p<0.01). Short-, mid- and long-term mortality were higher in patients with CIN (p<0.001). Independent predictors of CIN were CKD (Odds Ratio [OR] 3.41 95% Confidence Interval [CI] 1.81-6.41 p=0.001), anterior acute MI (OR 2.72 95%CI 1.55-4.77 p<0.001), diabetes (OR 2.47 95%CI 1.39-4.439 p=0.002), prior MI (OR 2.34 95%CI 1.29-4.27 p=0.005), age (OR 1.04 95%CI 1.01-1.07 p=0.007), Killip class (OR 1.36 95%CI 1.06-1.73 p=0.015) and haemoglobin values (OR 0.85 95%CI 0.74-0.98 p=0.028).

Conclusions: CKD, anterior acute MI, diabetes, prior MI, age, Killip class and haemoglobin at admittance were independent predictors of CIN in STEMI patients undergoing primary PCI. These predictors allow appropriate risk stratification before the procedure allowing the implementation of possible preventive approaches. Also, they could be used to refine the inclusion criteria for trials assessing the effects of interventions aiming to reduce the risk of CIN among patients with STEMI.

P1630 | BEDSIDE

Impact of coronary collaterals on long term outcome in patients undergoing primary angioplasty for ST elevation myocardial infarction

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Purpose: Coronary collaterals (CC) provide an alternative source of blood supply to myocardium jeopardized by occlusive coronary artery disease and they preserve myocardial function in the setting of a chronic total coronary occlusion. The effect of CC to occluded coronary arteries during ST-elevation myocardial infarction (STEMI) is still unclear. We examined the effect of collateral flow on clinical outcomes in patients undergoing primary angioplasty for acute myocardial infarction (AMI).

Methods: We studied 790 consecutive patients (483 m, 307 f, age 64.35±13.70 years), Primary PCI was performed according to standard clinical Practice. Collateral flow to the infarct-related artery was graded according to the Rentrop classification: 38% with grade 0 (no visible filling of any collateral channel), 36% grade 1 (filling of the side branches of the infarct-related artery), 16% grade 2 (partial filling of the epicardial vessel of the infarct-related artery), and 10% grade 3 (complete collateral filling of the epicardial vessel). Patients were divided into two groups: group A (patients with Rentrop grade 0 and 1) and group B (patients with Rentrop grade 2 and 3). Patients were subject to a 2-years clinical follow-up. Our endpoints were cardiac death, nonfatal reinfarction, and repeat myocardial revascularization. A combined endpoint (composite), defined as the occurrence of any endpoint (cardiac death or reinfarction or repeat revascularization) was also analyzed.

Results: Our study revealed that: 1) there are no statistically significant difference concerning the prevalence of risk factors in both groups, 2) in group B, there was a increased time of repertusion, but not enough to reach statistical significance 3) CC have a better development in patients with a history of ischemic heart disease. In particular, there was no correlation between Rentrop grade and diabetes mellitus (p=0.77) and peak cardiac enzyme elevation (p=0.48). The study showed an inverse correlation between the presence of anterograde flow measured before the procedure according to the TIMI flow scale and the development of CC. We could not find a significant impact of Rentrop grade on improvement of left ventricular ejection fraction after PCI (p=0.78), mortality (p=0.86) and major adverse cardiovascular events (p=0.88).

Conclusions: Our study showed no relationship between the degree of CC and long-term prognosis in patients after AMI. Coronary collateral circulation does not
P1631 | BENCH
The ratio of contrast volume to glomerular filtration rate predicts in-hospital and 6-month mortality in patients undergoing primary angioplasty for STEMI elevation myocardial infarction

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Purpose: To present the ratios of contrast volume to glomerular filtration rate (V/GFR) in patients with acute myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). We reported a total of 645 patients is prospectively enrolled. The study population was divided into tertiles based on V/GFR. A high V/GFR was defined as a value in the third tertile (>3.7). Patients in Tertile 3 had older age, higher rate of smoking, diabetes mellitus and contrast induced nephropathy, lower LVEF, hemoglobin, systolic and diastolic blood pressure. 19 patients died in hospital and 34 patients died during 6 month follow up. V/GFR was found as an independent predictor of in-hospital mortality (HR 1.07, 95% CI 1.04-1.12, p<0.001) and 6 month mortality (HR 1.08, 95% CI 1.02-1.15; p<0.003) (Table 1). We found a significant predictor for high CV/e-GFR for two different end points. While the ratio of 3.6 predicted in hospital mortality with 78% sensitivity and 82% specificity, the ratio of 3.3 predicted 6 months mortality with 71% sensitivity and 76% specificity.

Conclusions: High V/GFR level is associated with increased in hospital and long-term mortality in patients with STEMI undergoing primary PCI.

P1632 | BENCH
Correlation of health related quality of life with biomarkers and mortality in patients with STE-selective elevation myocardial infarction undergoing percutaneous coronary intervention

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Purpose: Numerous studies have analyzed the impact of quality of life on primary percutaneous coronary intervention (pPCI). In patients with acute STEMI the post PCI myocardial infarction (STEMI), yet little is known about the effect of the measured health related quality of life (HRQoL) on hard clinical endpoints.

Methods: This was a prospective observational trial focused on assessment of HRQoL in STEMI patients treated with pPCI. Three well-recognized HRQoL tools were used including: a generic (EQ-5D) and cardiac-specific (QLI, MacNew). HRQoL was measured at three time points: before pPCI, 2 hours after and on Day 4. The biochemical markers were measured at Day 1 and in-hospital mortality was recorded. Pearson’s correlation coefficient was calculated. The ROC analysis was performed to evaluate the optimal cut-off value.

Results: 103 STEMI patients were included in the study with mean age of 62 years (SD: 11.9), 27.2% of women, BMI 1.89 kg/m² (SD: 4.27), 49% treated from femoral access and 51% from radial access. The baseline HRQoL by EQ-5D VAS was 50 (SD: 22) that improved by 16.7 (+37%, p<0.001) after PCI. The mean EQ-5D health utility score 2 hours and 4 days after PCI were 0.46 (SD: 0.291) and 0.79 (SD: 0.248), respectively (p<0.01). The serum levels of NT-proBNP were inversely correlated with EQ-5D VAS (r=-0.348, p<0.05) and EQ-5D health utility score on Day 4 (r=-0.322, p<0.05). There was a correlation between in-hospital mortality and two MacNew domains: physical (r = -0.329, p<0.05) and emotional (r = -0.374, p<0.01).

Conclusions: The HRQoL is decreased in the acute phase of STEMI. The level of impairment seems to be correlated with the hard clinical outcomes including level of NT-proBNP and in-hospital mortality, which may suggest usefulness of HRQoL measurement in risk prediction models in STEMI population.
P1635 | BEDSIDE

Predictive value of elevated D-dimer in patients undergoing primary angioplasty for ST elevation myocardial infarction

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The aim of this study was to evaluate the prognostic value of D-dimer in patients with STEMI undergoing primary percutaneous coronary intervention (PCI). The prognostic value of D-dimer has been documented in patients with acute coronary syndrome without ST-segment elevation. However, its value in acute ST-segment elevation myocardial infarction (STEMI) remains unclear. We prospectively enrolled 453 consecutive STEMI patients (mean age 55.6±12.4 years, 364 male, 89 female) undergoing primary PCI. The study population was divided into tertiles based on admission D-dimer values. The high D-dimer group (n=151) was defined as a value in the third tertile (≥0.72 µg/ml fibrinogen equivalent units (FEU)), and the low D-dimer group (n=302) included those patients with a value in the lower two tertiles (<0.72 µg/ml FEU). Clinical characteristics, in-hospital and 6-month outcomes of primary PCI were analysed. The patients of the high D-dimer group were older (mean age 60.1±13.5 vs. 52.4±10.6, P<0.001). Higher in-hospital cardiovascular mortality and 6-month all-cause mortality rates were observed in the high D-dimer group (7.2 versus 0.6%, P<0.001) and by Cox multivariate analysis; a high admission D-dimer value (>72.0 µg/ml FEU) was found to be a powerful independent predictor of 6-month all-cause mortality (odds ratio: 10.1, 95% confidence interval: 1.24–42.73, P<0.001). These results suggest that a high admission D-dimer, level was associated with increased in-hospital cardiovascular mortality and 6-month all-cause mortality in patients with STEMI undergoing primary PCI.

P1636 | BEDSIDE

PCI in patients with and without prior CABG in a large monitor-controlled registry: changes over the past decade

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Background: Percutaneous coronary intervention (PCI) after prior coronary artery bypass surgery (CABG) is considered more complex, less successful, and characterized by more complications. Methods: Since 1996 invasive and interventional procedures of 130 institutions with annually over 20,000 PCI procedures are documented in a monitor-controlled registry. We analyzed the results of PCI in 2002 (n=18,822) compared to 2012 (n=21,512). Results: While the number of PCI patients with prior CABG was 7.6% in 2002 it continuously decreased to 2.2% in 2012 (p<0.001). The procedural differences of patients with no prior CABG and those with prior CABG are depicted in the table.

P1637 | BEDSIDE

Percutaneous coronary intervention in STEMI and more 305

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Aims: The final frontier of coronary percutaneous coronary intervention (PCI) remains the recanalization of chronic total occlusions (CTOs). One of the reasons for the low application rates of CTO-PCI by most physicians may be uncertainty concerning the success rate of the procedure. Improved guidelines for case selection may favourably impact these rates. Methods and results: Between 2012 and 2013, 156 eligible patients who were scheduled for percutaneous recanalization of a true CTO were included prospectively in the study. 98 patients underwent computed tomography (CT). By protocol we pre-defined the same 10 CTO key characteristics by conventional angiography (CA) and CT based on previously published independent predictors of failure and our team experience. Two experienced interventional cardiologist and two imaging specialists, respectively, analysed CTO characteristics. Prospectively the Japanese-CTO score of complexity was calculated. The mean age was 62±10 years old. According to the CA-Japanese-CTO score of complexity 51% of lesions was classified as difficult or very difficult. By CA 52% were severe calcified lesions. In most cases (88%) the strategy was antegrade. 58% performed with a TF catheter. By CA, the total stent length implanted per lesion was of 33.5±10.2mm (2.6±0.4 scaffolds per lesion). In all cases the first generated DES was implanted. Successful guidewire crossing was 86.4% and the overall success rate was 84.5%. Severe calcification by CA (37.5% vs. 11.5%, p<0.001) and by CT-scan (<50% cross sectional area) (26.6% vs. 60.0%, p=0.016) was more prevalent in failed cases. In multivariable logistic regression, the only independent predictor of procedural individual failure was the J-CTO score (odds ratio (OR) 2.5, 95% confidence interval (CI) 1.3-4.59, p=0.003, for each unit increase in J-CTO score) and silent ischemia as baseline clinic status before PCI-CTO (OR 4.71, CI 2.3-17.95, p<0.02).

Conclusions: According to the results of this prospective study, in our current era, the information provided by CA-J-CTO score; provide a significant impact in procedural results. Moreover silent ischemia as baseline clinical status was found as an independent predictor of failure of PCI for CTO. Further studies with higher sample size are required to determine whether new CA anatomic characteristic as 'bad landing zone' may improve case selection.

P1638 | BEDSIDE

Interaction between access site and antithrombotic therapy and impact on bleeding outcomes in STEMI

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Purpose: In the emergent setting of ST-elevation myocardial infarction (STEMI), aggressive antithrombotic therapy is routinely employed and major or minor bleeding is primary concern as percutaneous coronary intervention (PCI). We therefore sought to compare differences in bleeding outcomes among patients undergoing TRI and TFI for STEMI at a high-volume tertiary centre.

Methods: We conducted an observational study of 1052 patients with STEMI undergoing primary PCI at a high-volume tertiary medical centre from January 2008 to April 2010. The definition of major bleeding include the cumulative occurrence within 30-day after PCI of intracranial or intracardiac bleeding, haemorrhage at the access site requiring intervention, haematoma with a diameter of at least 5 cm, a reduction in haemoglobin levels of at least 4 g per decilitre without an overt bleeding source or at least 3 g per decilitre with such a source, re-operation for bleeding, or transfusion of a blood product. Minor bleeding was defined as any bleeding which did not meet the above major bleeding criteria. Results: GP IIb/IIIa inhibitor was used in 498 (47.3%) STEMI patients. Proportion of use of GP IIb/IIIa inhibitor was significantly higher in the transradial coronary intervention (TRI) group compared with the transluminal coronary intervention (TFI) group (78.5% vs. 68.5%, p<0.001). Major bleeding was seen more in the TRI group than TFI group (5.6% vs. 3.3%, p=0.08), which was not statistically significant. There was no difference of minor bleeding (1.7% vs. 1.7%, p=0.09) between TRI and TFI groups. In GP IIb/IIIa inhibitor used group (N=498), major bleeding was seen in 3.6% and minor bleeding was seen in 8.6%, however, no bleeding complications were seen in group without GP IIb/IIIa inhibitor use (N=554).

Conclusions: GP IIb/IIIa Inhibitor use was more liberal in radial access patients, reflecting a trend towards increased major bleeding in radial access patients. GP IIb/IIIa Inhibitor use was the strongest predictor of bleeding, independent of access site in patients with STEMI.
**P1642 | BEDSIDE**

Effect of intracoronary injection of autologous bone marrow derived progenitor cells on the global longitudinal strain in patients with STElevation myocardial infarction

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**Introduction:** The global longitudinal strain (GLS) is an important prognostic marker in myocardial infarction (MI). We studied the effect of intracoronary injection of autologous bone marrow derived progenitor cells (APC) on the GLS in STElevation myocardial infarction (STEMI). There is few data on this subject.

**Methods:** Prospective randomized study with recruitment of STEMI patients with: a) previous MI or major coronary events with a CPK peak ≥ 1.96 SDU; (2) within primary percutaneous coronary intervention (PCI) in the first 12 hours of MI (January 2011-May 2013). Patients were randomized 1:1 to intracoronary injection (in the first 7 days of MI) or not (controls) of APC. All received optimal medical therapy. A transhesive echocardiogram was performed in the first 3 days of MI and repeated at 6 to 12 months, with calculations of the left ventricle ejection fraction (LVEF) using the biplane Simpson’s method, and the GLS using the 2D semi-automatically method (average of all segments regional strain). Exclusion: poor eucardiochronic window (3) and lost of follow-up (5). The baseline characteristics and the changes in LVEF and GLS were compared between groups (x² and Mann-Whitney tests).

**Results:** In our sample of 34 patients (91% male, 50.9±9.5 years, 53% hyperten- sion, 50% dyslipidemia, 14% diabetes), 19 received APC and 15 were controls. No differences were found in baseline characteristics, including LVEF and GLS (Table). The LVEF and the GLS improved in both groups; (the GLS but not LVEF improvement) was significantly greater in the APC group.

**Conclusion:** The intracoronary APC injection in STEMI patients was associated with a greater improvement in GLS. In this context, the GLS might be more sensitive than LVEF for left ventricle systolic function assessment.

**P1641 | BENCH**

Novel bioactive oxidized phospholipids are produced in myocardium during ischemia reperfusion and act as mediators of cell death within cardiac myocytes

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A major therapeutic aim for myocardial infarction is early “reperfusion” of ischemic tissues. The process of ischemia followed by reperfusion (IR) causes an intense oxidative burst that results in cellular dysfunction and oxidizes intracellular molecules. Little is known about the impact oxidative stress on lipids within cardiomyocytes and their role in ischemic cell death. Using both in vivo and in vitro models of IR, our goal was to identify oxidized phospholipids generated and to determine their impact on cell viability. The rat coronary ligation model was used for 1 hr of ischemia then 24 hrs of reperfusion. 2D echocardiography and troponin-I assay were performed to assess myocardial damage. Myocardial lipid extracts underwent lipidomic analysis with high performance liquid chromatography linked to mass spectrometry to quantify 82 distinct OxPC species, as either fragmented or non-fragmented species. Lipid extracts of post-natal rat cardiac myocytes exposed to hypoxia and reoxyn- genation were analyzed to determine OxPC levels. Cell viability was determined in absence and presence of known OxPC molecules (POPCV and PONPC) and non-oxidized PSPC.

The role of IR injury lipidomics analysis revealed a significant increase in total OxPCs after 1 hr of IR (2.06±0.34 fold vs sham, p<0.05). This increase was also seen in fragmented OxPCs (1.85±0.18 fold, p<0.05) and non-fragmented OxPCs (1.96±0.26 fold, p<0.05). After 24 hrs of IR there was a significant sustain- ing decrease of fragmented OxPCs (1.80±0.22 fold, p<0.05). Cardiomyocytes under IR conditions also demonstrated significant increase in total OxPCs (5.23±0.99 fold vs control, p<0.05) and in fragmented aldehyde species (1.52±0.11 fold, p<0.05) correlating with decreased cell viability. Exogenously added fragmented OxPCs such as POPC and PONPC resulted in a significant loss of cardiomyocyte viability after 4 hrs of exposure when compared to control non-oxidized PC, PSCP (46.8±5, 40.5±5, respectively, vs 9.3±3.5 PSSP, p<0.05). Exposure of cardiomy- ocytes to POPC and PONPC resulted in increased mitochondrial permeability and DNA fragmentation.

This study is the first time that OxPCs are generated within myocardial tis- sue during IR and they have detrimental effects on cardiomyocyte viability. Since there are no current therapies for IR in clinical practice, fragmented OxPCs repre- sent a novel therapeutic target to attenuate myocardial injury during IR.
P1644 | BENCH
Cyclosporine A but not postconditioning reduces microvascular damage after coronary ischemia and reperfusion
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Purpose: Postconditioning and cyclosporine A prevent mitochondrial permeability transition pore opening. The effect of postconditioning versus cyclosporine on microvascular damage following coronary ischemia/reperfusion is unknown.

Methods: Pigs subjected to coronary occlusion for 1h followed by 3h of reperfusion were assigned to control (n=8), postconditioning (n=9) or cyclosporine A intravenous infusion 10-15 min before the end of ischemia (n=8). Postconditioning was induced by 8 cycles of repeated 30-s balloon inflation and deflation. After 3h of reperfusion magnetic resonance imaging, triphenyltetrazolium chloride/Evans blue staining and histopathology were performed. Microvascular obstruction (MVO, % of gadolinium-enhanced area) was measured early (3 min) and late (12 min) after contrast.

Results: Infarct size with double staining was smaller in cyclosporine (44.7±7.1%, P=0.017) but not postconditioning pigs (50.1±7.2%, P=0.28) versus controls (54.4±4.7%). Late-MVO was significantly reduced by cyclosporine (14.2±5.8%) but not postconditioning (24.4±5.5%) when compared with controls (32.5±5.6%) (Figure). The late-to-early MVO ratio was lower in cyclosporine (0.42±0.19, P<0.0001) and postconditioning pigs (0.55±0.20, P=0.011) than in controls (0.81±0.07). Determination of left ventricular ejection fraction at baseline and 3h of reperfusion was smaller in cyclosporine (7.9±2.2%, P<0.015) but not postconditioning (-13.2±6.3%, P=0.62) when compared with controls (-15.6±3.7%). Erythrocyte stasis was higher in MVO (4.4±4.5%) versus gadolinium-hyperenhanced region (0.3±1.1%, P<0.001).

Conclusions: Cyclosporine A infusion but not postconditioning had a beneficial effect on microvascular damage and was associated with smaller infarct size and better preserved LV function when compared with controls.

P1645 | BENCH
Electron transport chain properties of mitochondria from left ventricle hypothyroid hearts as a substrate for increased vulnerability to ischemia-reperfusion
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Purpose: Left ventricular hypothyroidism (LVH) is associated with a resistance to some forms of cardioprotection (1,2). Mitochondrial defects arising during ischemia set the stage for a subsequent reperfusion injury (3). There appear to be no studies comparing the effects on mitochondrial ischemia itself, as opposed to ischemia-reperfusion, in normal and LVH hearts. We have studied the effect of ischemia on mitochondria from rats with LVH to shed light on possible mechanisms of this resistance.

Methods: Hearts isolated from WKY (control) and SHR-SR (LVH) rats were subjected to 35 min normoxic perfusion or global ischemia and mitochondria were prepared immediately thereafter. Cytochrome c and b content and complex III (CIII) activity were measured spectrophotometrically. H2O2 production was determined by Amplex assay. Protein carbonylation was measured by western blotting as a product of 2,4-dinitrophenylhydrazine reaction. P<0.05 was considered significant.

Results: LVH was manifest in SHR-SR rat hearts (heart weight/body weight ratio (x 1000) 3.43±0.05 vs 2.35±0.03 in WKY, n=40). Cytochrome c/b ratios in WKY hearts were 0.938±0.057 and 0.989±0.043, n=7, and in SHR-SR hearts 0.857±0.100 and 1.005±0.091, n=8 following normoxia and ischemia, respectively. Normoxic SHR-SR hearts showed a markedly higher CIII activity than WKY hearts (368.1±37.3 vs 144.02±14.1 nmol/mg/min, n=8; 422.6±52.1 vs 203.6±12.5 mmol/mg/min, n=6). Ischemia decreased CIII activity in SHR-SR hearts to 47.8±5.9%, n=9. A non-significant decrease (to 69.5±7.8%, n=7) was also found in WKY hearts. H2O2 production, when measured with a mixture of Cl (malate, glutamate) and CII (succinate) substrates, was decreased in postischemic mitochondrial in WKY as well as SHR-SR hearts in the absence of rotenone, but in the presence of antimycin A. There appeared to be a trend (p<0.08) to a lower H2O2 production in SHR-SR vs WKY hearts after normoxia. There was no difference in the level of protein carbonylation between any of the conditions.

Conclusions: The present data suggest that the ETC activity in LVH differs from normal hearts under normoxia (higher complex III activity and lower H2O2 production) and may be more vulnerable to ischemia (greater apparent damage to complex III activity). Further work is needed to determine whether these differences go some way to explain greater vulnerability of LVH hearts to ischemia-reperfusion.

P1646 | BENCH
C-type natriuretic peptide reduces ischemia-reperfusion-induced activation of mast cells and microcirculatory leakage
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Purpose: During postischemic reperfusion, the activation of mast cells (MC) is an important mediator of reperfusion injury (1). Due to pleotropic effects released from MC the tissue damage. It is unclear whether and how atrial (ANP) and C-type natriuretic peptides (CNP) regulate the activity of MC and, thereby, influence ischemia-reperfusion-induced disruption of the microvascular barrier.

Methods: Intravital microscopy was used to visualize the microcirculation within cremaster muscles. The cremasteric tissues were exposed to 20 min global ischemia followed by 20 min reperfusion. A intravenous infusion of 10-15 min before the end of ischemia (n=8). Postconditioning pigs (0.55±0.07) to a lower H2O2 production in SHR-SP vs WKY hearts after normoxia. Late-MVO was significantly reduced by cyclosporine (14.2±5.8%) but not postconditioning (24.4±5.5%) when compared with controls (32.5±5.6%) (Figure). The late-to-early MVO ratio was lower in cyclosporine (0.42±0.19, P<0.0001) and postconditioning pigs (0.55±0.20, P=0.011) than in controls (0.81±0.07). Determination of left ventricular ejection fraction at baseline and 3h of reperfusion was smaller in cyclosporine (7.9±2.2%, P<0.015) but not postconditioning (-13.2±6.3%, P=0.62) when compared with controls (-15.6±3.7%). Erythrocyte stasis was higher in MVO (4.4±4.5%) versus gadolinium-hyperenhanced region (0.3±1.1%, P<0.001).

Conclusions: Cyclosporine A infusion but not postconditioning had a beneficial effect on microvascular damage and was associated with smaller infarct size and better preserved LV function when compared with controls.

P1647 | BENCH
Cigarette smoking negates the beneficial effect of ischemic postconditioning in limiting the infarct size through insufficient activation of AKT and eNOS
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Introduction: Cigarette smoking is one of the risk factors for cardiovascular disease. Conditioning (either PreC- or PostC-) ameliorates injury that occurs upon reperfusion (rep) following myocardial ischemia (isc). The endogenous protective pathways are silenced by a number of co-morbidities, ageing and possibly by detrimental habits such as cigarette smoking.

Purpose: To investigate the effects of exposure to cigarette smoke on isc/rep injury and its potential interference with ischemic conditioning.

Materials and methods: C57BL/6 male mice were divided in 2 groups. The Cigarette Smoking group (CS), was exposed to cigarette smoke from reference cigarettes (SRK University of Kentucky, USA) 4 times a day for 4 weeks. The Control group was exposed to room air (RA). Animals from both groups were subjected to 30 min regional myocardial ischemic following 2 hours of rep with the following interventions: RA and CS groups: Control, no further intervention, 2) PreC: 5 min min ischemic rep before index isc and 3) PostC: 3 cycles of 10 sec ischemic rep applied immediately after index isc. The infarct size (i) and the area at risk (R) were estimated as i/R. In a second series of experiments additional animals were subjected to the above interventions up to the 10th min of rep when the ischemic part of the myocardium was excised for biochemical measurements.

Results: Exposure to cigarette smoke did not increase the infarct size compared to the air exposed group (38.3±3.6% vs 40.9±2.2% respectively, P=NS). Application of PreC was beneficial in saline (CS:12.1±1.6%) and RA (17.9±1.8%), p<0.05 vs no PreC controls. PostC failed to limit infarct size in CS animals, while the beneficial effect of PostC was preserved in RA mice (43.3±2.2% vs 17.0±2.7%, P<0.05). PreC in both groups and PostC in the RA group lead to in-
creased phosphorylation of AKT activation, whereas PostC failed to do enhance p-AKT in the CS group. Total AKT levels remained unchanged among groups. eNOS phosphorylation was evident in the CS group to a significantly higher extent in preconditioned RA and CS groups, as well as in PostC RA group.

**Conclusion:** Short term exposure to cigarette smoke does not per se increase infarct size. In addition, ischemic preconditioning functions in mice exposed to cigarette smoke, possibly through activation of AKT and eNOS, whilst the post-conditioning benefit is lost in mice that have been exposed to cigarette smoke for 4 weeks.

**P1648 | BENCH**

**Changes in gene expression profiling of porcine myocardium after repetitive ischemia/reperfusion**

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**Background:** We have analysed the gene expression profile of the myocardium after repetitive ischemia/reperfusion aiming to simulate human pre-infarction angina pectoris in an animal model ready to translate.

**Methods:** Under general anaesthesia domestic pigs underwent closed chest repetitive (3x10 cycle) ischemia/reperfusion by percutaneous balloon occlusion/deflation of the mid left anterior descending coronary artery. Sham balloon occlusion/deflation was performed in control pigs (n=3). After 5h (n=3) and 24h (n=3) follow-up, five myocardial samples were harvested from the heart basis (LAD1) to apex (LAD5) including the border zone of the ischemia (LAD3) localized by using anatomical landmarks (below the origin of the 2nd diagonal branch). The hypoxia inducible factor-1 (HIF1alpha), caspase-3, GATA4 and myocyte enhancer factor 2C (MEF2C) gene expression patterns of the corresponding regions were analysed by using quantitative real-time PCR (RT-PCR).

**Results:** Repetitive ischemia/reperfusion resulted in a rapid increase in HIF1alpha and caspase-3 expression in the ischemic area and border zone, while increase in MEF2c expression was moderate. GATA4 expression was more pronounced 24h after the ischemic attack (Fig. 1).

**Conclusions:** Short periods of repetitive ischemia/reperfusion without infarction cause alteration in gene expression profile of the myocardium, which might be responsible for the protective effect against subsequent infarction and necrosis.

**P1650 | BENCH**

**Characteristics of vascular responses to drug eluting stents in rabbits: evaluated by optical coherence tomography and gene expression analyses**

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**Background:** Recent several clinical studies suggest that second-generation cobalt-chromium everolimus-eluting stents (CoCr-EES) lead to more favorable vascular responses than first-generation sirolimus-eluting stents (SES). However, it remains unclear the difference of vascular responses between CoCr-EES and SES.

**Methods:** A total of 42 stents (14 bare-metal stents [BMS], 13 CoCr-EES, and 15 SES) were deployed in the iliac arteries of 31 Japanese White rabbits. Optical coherence tomography (OCT) and quantitative real-time reverse transcription-polymerase chain reaction (QRT-PCR) analyses of the neointima were performed on days 30 and 90 after the stent implantation. OCT showed that CoCr-EES and BMS had a more favorable strut coverage than the SES at both 30 and 90 days after the implantation. The SES showed significantly less neointimal thickening than the CoCr-EES and BMS on day 90 (SES, 0.077±0.037; EES, 0.108±0.046; BMS, 0.119±0.076 mm, P<0.001). In the QRT-PCR analyses, on day 30, the gene expression of the angiogenic growth factors (hepatocyte and basic fibroblast growth factors) and proteoglycans (decorin, biglycan and lumican) were more upregulated in the BMS than in the SES. However, at 90 days after stenting, the gene expression of proteoglycans and collagen was more upregulated in the SES than in the CoCr-EES and BMS.

**Conclusions:** CoCr-EES as well as BMS demonstrated a greater strut coverage than the SES. Compared to the CoCr-EES, the vascular healing-related gene expression was rather upregulated in SES in the late phase, representing an ongoing active vascular healing process. These differences may lead to different clinical outcomes in humans.
Methods: In group of patients with ST-acute myocardial infarction, we took samples from coronary sinus before primary PCI and after reperfusion, and peripheral venous samples after 6, 12 and 24 hours after PCI.

Results: The largest DNA damage detected by all methods (SSB, ENDO and FAD) was found before and immediately after PCI (31.2±18.1%/Tail DNA). After 6 hours we detected significant decrease of DNA breaks (16.1±4.5%/Tail DNA; p<0.05) and with more decrease DNA repair after 12 (12.1±6.9%/Tail DNA; p<0.0001) and 24 hours (13.8±6.9%/Tail DNA; p<0.0001).

Conclusions: Acute myocardial infarction is connected with DNA oxidative damage; we can measure oxidative damage using DNA endonuclease and formamidopyridin DNA glycosylase, with significant repair after 6, 12 and 24 hours.

Conclusions: Onset-to-balloon time within 3 hours reduces the risk of MACE in long term outcome.

Conclusion: Onset-to-balloon time within 3 hours reduces the risk of MACE in long term outcome.
P1656 | BEDSIDE
Lower in-hospital mortality in STEMI patients with postponed angioplasty after successful pre-transfer medication compared with primary angioplasty. RO-STEMI registry data
G.P. Tatu-Chitoiu1, D. Deleanu2, A. Petris3, C. Macarie4, L. Petrescu5, C. Arsenescu Georgescu6, R. Cîmpeanu7, I. Tilea7, R. Capulăneanu8, D. Vinereanu8 on behalf of RO-STEMI investigators.
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Background: A national program for interventional therapy in STEMI pts was opened in August 2010 in Romania. In real life it is difficult to perform primary angioplasty within the first 3 h, 51.6% within 6 h, 68.2% within 12 h, 79.1% within 24 h of onset of symptoms. Primary percutaneous coronary intervention (PCI) and 71.1% with ST elevation myocardial infarction (STEMI), 24.7% were admitted used an ambulance as transportation to the hospital. Among 7442 patients with non ST elevation myocardial infarction (NSTEMI), respectively. Among 3032 patients (28.9%) with non ST elevation myocardial infarction of onset of symptoms. Primary percutaneous coronary intervention (PCI) and 4.6% and 3.8% for STEMI and NSTEMI, respectively. The RO-STEMI registry data suggest that a postponed PCI strata-
Objective: To compare the in-hospital mortality in STEMI pts treated in Romania between January 1, aspirin, clopidogrel, and unfractionated heparin and with/without thrombolysis is recommended.
Methods: A STEMI network consisting in 14 PCI centers and a large scale pharmaco-invasive approach is the strategy of the Romanian national program. According to our protocol, pts with FMC-to-PCI time estimated within 2 hours are directly transported to the one of the 14 PPCI centers. In 1 pts with a FMC-to-PCI longer than 2 hours pre-transfer thrombolysis is strongly recommended. Aspirin, clopidogrel and unfractionated heparin are also recommended for all pts. PPCI or rescue PCI are performed in all pts with persistence of the chest pain and of the ST-segment elevation at admission in the PCI center. For pts with cessation of the chest and more than 50% ST-segment resolution the PCI center person nel have the liberty to perform PCI immediately after admission or to postpone PCI for the next 3 to 48 pts. Pts data are recorded in the Romanian registry of STEMI (RO-STEMI registry).
Results: A total of 15659 pts were recorded in the RO-STEMI registry in 2012 and 2013. The lowest in-hospital mortality (1.98%) was seen in pts with postponed PCI (N=808) followed by PPCI (4.35%, N=7253), rescue PCI (4.43%, N=856), thrombolysis only (9.93%, N=1321, and pts not undergoing reperfusion (14.86%, N=579). The differences between postponed PCI versus PPCI and postponed PCI or PPCI or rescue PCI versus thrombolysis alone or not undergoing reperfu-
Conclusions: The RO-STEMI registry data suggest that a postponed PCI strat-

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P1657 | BEDSIDE
A large-scale prospective cohort study on the current status of therapeutic modalities for acute myocardial infarction in China: initial results of the China Acute Myocardial Infarction Registry
J.G. Yang, Y.J. Yang, X.J. Gao, H.Y. Xu, Y. Wu, L. Song, W. Li, Y. Wang, X.R. Tang, L. Chen on behalf of China Acute Myocardial Infarction Registry. Cardiovascular Institute & Fujii Hospital, Beijing, China, People's Republic of China
Objective: Little is known about the management of acute myocardial infarction (AMI) in the real world in China. The purpose of this study was to build a compre-
Methods: Among 30 provinces, municipalities or autonomous districts in China, at least one tertiary and secondary hospital was selected. Between January 2013 and November 2013, we consecutively registered all patients with AMI within 7 days after the onset of AMI in 93 participating medical institutions. A standardized case report form was used to register all the patients.
Results: A total of 310 STEMI and 1310 non-STEMI cases were registered (7784 men, 74.3%; 2690 women, 25.7%) with an age of 61±18 years. Only 1153 (11.0%) patients used an ambulance as transportation to the hospital. Among 7442 patients (71.1%) with ST elevation myocardial infarction (STEMI), 24.7% were admitted within the first 3 h, 51.6% within 6 h, 68.2% within 12 h, 79.1% within 24 h of onset of symptoms. Primary percutaneous coronary intervention (PCI) and thrombolysis were conducted for 3312 (43.8%) and 842 patients (11.1%), respec-
Conclusions: IH-MI are present in about 3% of all STEMI in current clinical prac-
tice. We did not observe a change in IH-MI occurrence during our observational period. Patients with an IH-MI were older and presented more often in cardiogenic shock. Their in-hospital time to treatment was longer, however, total ischemic time (symptom onset to angio time) was shorter compared to non IH-MIs. Invasive diag-

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P1658 | BEDSIDE
In-hospital myocardial infarction: incidence, patient characteristics and clinical outcome: results from a 10 year single-centre myocardial infarction registry
R. Zahn1, S. Camci1, K. Batz1, A. Bernhardt2, A.K. Gitt1, B. Mark1, R. Winkler1, C. Kilikowski1, T. Kleemann1, U. Zeymer1, A.K. Gitt1, B. Mark1, 1Clinical Center of Ludwigshafen, Ludwigshafen am Rhein, Germany; 2Heart Attack Research Center, Ludwigshafen am Rhein, Germany
Background: Acute ST elevation myocardial infarction (STEMI) occurring in pa-
tients while being already in a hospital (in-hospital myocardial infarction), is rarely given sufficient consideration and is also poorly characterised.
Methods: We retrospectively analysed all patients with an acute STEMI who were treated at our hospital between 2000 and 2009 (MIIRLU-Registry).
Results: Between 6/2000 and 12/2009 3143 patients with an acute STEMI were included in our database. An IH-MI was present in 90 (2.9%) of these patients. The proportion of ICH-MI did not change from 2000-2009 and varied between 0.3 and 4.4% per year.

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P1659 | BEDSIDE
Management of multivessel coronary disease in STEMI patients; a systematic review and meta-analysis
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Introduction: Appropriate management for patients with multi vessel coronary disease presenting with St Segment Elevation Myocardial Infarction (STEMI) re-
mains to be defined.
Methods: Medline and Cochrane Library were searched for randomized con-
trolled trials (RCTs) or observational studies adjusted with multivariate analysis reporting about STEMI patients with multivessel coronary disease treated with culprit only or with complete revascularization, excluding those in cardiogenic shock. Prespecifed analysis were performed according to strategy of complete revascularization, either during the same procedure of primary Percutaneous Coronary Intervention (PCI) or during index hospitalization. MACED (death or myoc-

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Table: IH-MI (n=90) no IH-MI (n=3053) p value

<table>
<thead>
<tr>
<th>IH-MI (%)</th>
<th>no IH-MI (%)</th>
<th>p value</th>
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<tr>
<td>Age (years)</td>
<td>69.4±11.8</td>
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<td>Men (%)</td>
<td>34%</td>
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<td>Underlying heart disease (%)</td>
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<td>Left bundle branch block (%)</td>
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<td>Reperfusion therapy (PCI/CABG) (%)</td>
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<td>Hospital death (%)</td>
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</tbody>
</table>

Conclusions: IH-MI are present in about 3% of all STEMI in current clinical prac-
tice. We did not observe a change in IH-MI occurrence during our observational period. Patients with an IH-MI were older and presented more often in cardiogenic shock. Their in-hospital time to treatment was longer, however, total ischemic time (symptom onset to angio time) was shorter compared to non IH-MIs. Invasive diag-

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P1660 | BEDSIDE

Similar 3-year-mortality in patients with STEMI and NSTEMI for known as well as for newly diagnosed diabetes - Results of the SWEETHEART Registry


on behalf of SWEETHEART Study Group. 1Heart Attack Research Center at the University of Heidelberg, Ludwigshafen am Rhein, Germany; 2Herzzentrum Ludwigshafen, Med. Klinik B, Kardiologie, Ludwigshafen am Rhein, Germany; 3Institut f. Herzinfarktfororschung Ludwigshafen, Ludwigshafen am Rhein, Germany; 4Institute for Cardiovascular Pharmacology & Epidemiology, Mahlow, Germany; 5Heart and Diabetes Center NRW, Bad Oeynhausen, Germany

Background: Joint ESC/EASD guidelines recommend testing for diabetes (DM) using oral glucose tolerance test (OGTT) in patients with CAD.

Methods: The SWEETHEART-registry enrolled 2,767 consecutive patients (pts) with STEMI or NSTEMI to identify abnormal glucose metabolism and to document outcome. In pts without DM, OGTT was performed at day 4 after the MI. We examined the impact of known and newly diagnosed DM (new DM) on 3-year-outcome.

Results: OGTT detected 16.0% new DM in STEMI and 17.8% in NSTEMI. Pts with new DM were younger and suffered from less concomitant diseases. 3-year-mortality rates were high, both for known and for new DM, without differences with new DM were younger and suffered from less concomitant diseases. 3-year-mortality was similar for known and new DM.

Conclusion: OGTT after acute MI identified new DM in 16.0% of STEMI and 17.8% of NSTEMI pts. For known and new DM, 3-year-mortality was similar for STEMI and NSTEMI.

P1661

P1662 | BEDSIDE

Impact of preinfarction angina on one-year mortality in STEMI patients undergoing primary PCI


Purpose: It has been postulated that patients with ST-segment elevation myocardial infarction (STEMI) who experience preinfarction angina might have smaller infarct size and better prognosis. Our goal was to evaluate impact of preinfarction angina on one-year mortality in STEMI patients undergoing primary percutaneous coronary intervention (primary PCI).

Methods: The study included 2266 patients with STEMI who underwent primary PCI in a high-volume center during the years 2010-2012. Patients with preinfarction angina (PA) had at least one episode of typical chest pain within 72h of presentation with STEMI and without preinfarction angina were compared with the log-rank test.

Results: Occurrence of preinfarction angina was reported in 69.5% of the studied population. Median time to reperfusion was significantly longer in patients with PA, as compared to patients without PA (285 minutes vs 249 minutes, p<0.001). The observed difference in the time to reperfusion was mainly due to the longer patient-related delay in patients with PA (165 vs 132 minutes, p<0.001). Health care system delay was similar in both groups (p=0.49). There was a trend towards lower levels of peak creatine kinase (CK) in patients with PA (1526 U/L vs 1715 U/L, p=0.09). Comparison of the Kaplan-Meier cumulative mortality curves with the log-rank test showed no significant difference between the two groups of patients (p=0.385).

Conclusion: Preinfarction angina in patients undergoing primary PCI is associated with longer time to reperfusion, mainly due to longer delays in presentation. There is a trend towards lower peak CK values in these patients, but one-year mortality is similar as in patients without preinfarction angina.

P1663 | BEDSIDE

Comparison of the prevalence of cardiovascular risk factors and clinical presentation at admission in patients with takotsubo cardiomyopathy and STEMI

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Background: The clinical presentation of Takotsubo cardiomyopathy (TTC) mimics acute myocardial infarction and is most often characterized by chest pain, ST segment elevation, cardiac enzymes increase and left ventricular dysfunction.

Purpose: The aim of the analysis was to compare the prevalence of cardiovas-
cultural (CV) risk factors in a population of patients (pts) with TTC and acute myocardial infarction with ST segment elevation (STEMI).

Methods: The analysis included 79 consecutive female pts diagnosed with TTC and 103 consecutive female pts with STEMI. In both groups compared the incidence of CV risk factors such as age, hypertension, diabetes mellitus, hypercholesterolemia, smoking cigarettes.

Results: The mean age of patients was 69.2 years in pts with TTC and 68.2 in the group of STEMI (p<0.05). Pts with TT had higher systolic blood pressure on admission (132.72 vs 124.14 mmHg, p<0.05), lower ejection fraction (41.78 vs 45.59, p<0.05), a lower concentration of TnI (3.78 vs 63.17, p<0.05) and CKMBmass (14.76 vs 181.51, p<0.05). There was no differences in heart rate at admission (80.2 vs 80.8 bpm).

There was no difference in the incidence of CV risk factors such as age, hypertension, hypercholesterolemia, smoking cigarettes, diabetes mellitus (p>0.05) in the group of pts with the TT and STEMI. In addition, in follow-up consisting of a maximum of 7 years any pt remaining in follow-up had acute coronary syndrome diagnosed and had not performed coronary revascularization.

Conclusion: In pts with TTC the incidence of CV risk factors was the same as in the group of STEMI pts. Pts with TTC had higher systolic blood pressure, lower ejection fraction, lower TnI and CKMBmass on admission.

P1664 | BEDSIDE
Comparison of complications between transradial approach and transfemoral approach for patients with ST-T segment elevation myocardial infarction
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Purpose: Some trials have suggested that transradial intervention (TRI) reduces vascular complications and bleeding compared with transfemoral intervention (TFI). In this study, we aimed to assess the feasibility of TRI in patients with ST-segment elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention (PCI).

Methods and results: This is a multicenter, retrospective observational study. Between January 2006 and December 2010, we investigated a total of 783 acute myocardial infarction (AMI) patients who underwent primary PCI. All of these patients, we reviewed 553 STEMI patients except using intra aortic balloon pumping (IABP) and percutaneous caldiopulmonary support device (PCPS) patients. TRI was performed in 174 patients and TFI was performed in 379 patients. Mean follow-up period was 25 months. Outcome measures were in-hospital complications (all-cause death, recurrent myocardial infarction, stroke, major bleeding) and major adverse cardiovascular events (MACE: cardiac death, target vessel revascularisation, recurrent myocardial infarction, admission of heart failure) at 3 years. During the initial hospitalisation, the complications rate was 1.1% in TRI group and 6.0% in TFI group (P=0.025). Kaplan-Meier survival curves showed that the freedom from MACE was 67.5% in TRI vs 68.0% in TFI at 3.8 years (P=0.74).

Conclusion: The in-hospital complications rate s were statistically lower in TRI group compared with TFI group, and TRI performed STEMI was feasible compared to TFI.

P1668 | BEDSIDE
Risk stratification for the development of heart failure after acute coronary syndrome at the time of hospital discharge: predictive ability of GRACE risk score

Objectives: Despite encouraging declines in the incidence of heart failure (HF) complicating acute coronary syndrome (ACS), it remains a common problem with high mortality. Being able to identify patients at high risk of HF after ACS would be of great clinical and economic impact. With this study, we assessed the usefulness of the GRACE score to predict HF after ACS.

Methods: We studied 4,137 consecutive patients discharged from a single center with diagnosis of ACS. We analyzed HF incidence, timing, and association with the follow-up mortality. Cox proportional hazards modeling was performed to assess the accuracy of the GRACE score risk to predict HF admissions in follow-up (median 3.1 years).

Results: 435 patients (10.5%) developed HF. GRACE score was an independent predictor of HF after ACS (HR 1.02, CI 95% 1.01-1.03, p <0.001). A risk gradient for the development of HF with GRACE risk score was shown (figure): high and moderate GRACE risk groups have been linked to a six- and two fold increased risk of HF. This risk gradient was maintained in patients with and without prior history of HF in STEMI and NSTEMI groups, and in patients with depressed and preserved LVEF. The development of HF was associated with high mortality (54.5% vs 13.4%; HR=4.48; 95% CI, 3.84-5.24; P<0.001). After adjusting for GRACE risk score, HF development resulted an independent predictor of mortality.

P1667 | BENCH
Incidence and predictors of stroke after an acute myocardial infarction: specific aspects during the early phase and after discharge from hospital
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Purpose: Stroke is a severe complication after an acute myocardial infarction (AMI), and is closely associated with a poor prognosis. The aim of the study was to evaluate the frequency, characteristics and factors associated with in-hospital and post-discharge stroke after AMI. Prognosis at one year was also assessed for in-hospital stroke.

Methods: Observational study, including 8485 consecutive patients admitted for AMI between January 2001 and June 2010. Among others major adverse cardiac events (MACE), both ischemic and hemorrhagic stroke events were recorded during one year follow up.

Results: 168 (2%) stroke were recorded during the first year of follow-up after AMI. Most patients (123/168 (73.2%)) had a stroke during the hospital stay, and 87% within the 5 days after admission. The mortality at 30 days was higher in patients with in-hospital stroke than in patients without stroke (34.1% vs. 7.6%, p<0.001). After multivariate logistic regression, in-hospital stroke were independently associated with age (OR: 1.04, 95% CI: 1.01-1.07, p=0.003), previous stroke (OR: 1.44, 95% CI: 1.04-1.98, p=0.017), new onset AF (OR: 1.6, 95% CI: 1.02-2.56, p=0.04), and CRP (OR 1.006, 95% CI: 1.003-1.009, p<0.001). A risk gradient for the development of HF after ACS (HR 1.02, CI 95% 1.01-1.03, p<0.001). During the ten years of inclusion, the annual rate of stroke after AMI remained stable.

Conclusions: The present study describes specific predictive factors for in-hospital stroke after AMI, with a high mortality rate. After discharge from AMI, stroke occurrence remains rare and mostly associated with a high cardiovascular risk.

P1668 | BEDSIDE
Outcome after MI in different socio-economic environments
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Purpose: To compare outcome and quality of secondary prevention in patients
after myocardial infarction (MI) of different socio-economic environments including patients from 3 teaching hospitals.

Methods: In this registry study, all patients hospitalized for MI (STEMI and NSTEMI with elevated troponin or CK-MB isoenzymes) in the year 2010 were included (exclusion criteria: Age over 75 years, survival less than 30 days after acute event, previous MI). Outcome data was extracted from treatment reports. Participation in a cardiac rehabilitation programme was quantified from questionnaires sent out in 2013. 3.5-year mortality was determined from mortality statistics and registration offices in 2013 and early 2014.

Patient characteristics of the different hospitals

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Switzerland</th>
<th>Poland</th>
<th>Ukraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients admitted with first ACS</td>
<td>137</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>59.0 ± 10.4</td>
<td>59.9 ± 9.9</td>
<td>60.4 ± 10.1</td>
</tr>
<tr>
<td>Females</td>
<td>26.5%</td>
<td>27.0%</td>
<td>27.4%</td>
</tr>
<tr>
<td>Smokers</td>
<td>49.3%</td>
<td>55.9%</td>
<td>73.5%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12.5%</td>
<td>22.3%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Obesity BMI &gt; 30</td>
<td>20.3%</td>
<td>33.3%</td>
<td>29.3%</td>
</tr>
<tr>
<td>PTCA</td>
<td>0.0%</td>
<td>0.0%</td>
<td>20.1%</td>
</tr>
<tr>
<td>3.5-year mortality</td>
<td>100%</td>
<td>92.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Returned Questionnaires (percent of total)</td>
<td>343 (62.7%)</td>
<td>204 (54.4%)</td>
<td>92 (56.8%)</td>
</tr>
<tr>
<td>Participation in Cardiac Rehabilitation (percent of returned questionnaires)</td>
<td>238 (69.4%)</td>
<td>105 (51.4%)</td>
<td>24 (26%)</td>
</tr>
</tbody>
</table>

Conclusions: There were substantial differences in treatment and secondary prevention measures according to low-, medium- and high-income socio-economic situation. These differences lead to a 4-fold difference in mortality. Countries with low socio-economic environment should be better supported to improve care in particular for MI patients.

P1669 | BEDSIDE
The association between the magnitude of hs-troponin decline and 12 month mortality outcome

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Purpose: An observed rapid fall in hs-troponin (hs-Tn) within the first 24 hours after the peak effect is commonly observed. However, the clinical significance is unknown. We explored the relationship between magnitude of hs-Tn drop and late mortality.

Method: A database of all patients with hs-Tn drawn across several hospitals between 2011-2012 was used. This allowed a minimum 12-month evaluated follow-up. All hs-Tn measurements were performed on the Roche Elecsys assay. Patients with no rise, continual rise and only with a single sample of hs-Tn were excluded. Mortality was assessed using the state mortality register. Patients were arbitrarily divided into 0-20% (Group 1), 21-50% (Group 2) and >50% drop (Group 3) in hs-Tn. Outcomes were compared in univariate and multivariate logistic regression.

Results: A total of 3,585 patients were available for analysis of which there were 2,270 in Group 1, 1,288 in Group 2 and 303 in Group 3. The mortality observed in Group 1 was 16.9% (430 patients), Group 2 14.7% (189 patients) and Group 3 8.1% (24 patients) (p=0.001). The median age of Group 1 was 80 years, Group 2 76 years and Group 3 65 years (p=0.001). Patients in Group 1 were more likely to have a lower baseline renal function (median eGFR = 52 ml/min/1.73m²), Group 2 (median eGFR =63ml/min/1.73m²) and Group 3 (median eGFR = 73mls/min/1.73m²) (p=0.001). After adjusting for the maximum troponin elevation and baseline renal function, the greater magnitude of hs-TnT decline was associated with a decrease in mortality at 12 months. (Group 2, OR=0.82 (CI=0.67-0.98, p=0.03)) and Group 3, OR=0.51 (CI=0.33-0.77, p=0.001). However after adjusting for age and renal function, this was no longer statistically significant (Group 2, OR=0.93 (CI=0.76-1.13, p=0.45), Group 3, OR=0.79 (CI=0.51-1.22, p=0.29)).

Conclusion: A rapid decline in hs-Tn has a better prognosis although this benefit might be explained by a younger age group.

P1670 | BEDSIDE
The evolution of high-sensitivity troponin-T in asymptomatic post-ACS patients who remained event free during 400 days follow-up

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Background: Limited data are available on high sensitivity (hs) Troponin T (TnT) and its evolution during one year follow-up in asymptomatic patients stabilised after acute coronary syndrome (ACS) admission.

Purpose: Describe 1-year hsTnT patterns in asymptomatic patients after ACS.

Methods: BIOMAC-CS is an observational study of ACS patients in 18 hospitals in our country. Treatment is left to the discretion of the physician. During 1 year follow-up, 20 repeat blood samples are taken at preset time intervals. Serum and plasma are separated and stored on site at -80°C within 2h, until batch analysis in the central laboratory of the Erasmus MC. This abstract describes 103 patients who remained free of death, readmission for ACS, coronary revascularisation and anginal symptoms until 400 days. We determined hsTnT with the Roche STAT on Cobas e system in their repeated samples.

Results: Mean age was 65 (SD 5) years, 79% were men, 64% had STE-ACS. Patient profile was typical for an ACS population. Discharge medication included antiplatelet therapy (99%) and statins (97%). Median peak hsTnT value within 7 days was 632 (IQR 192 to 1640) ng/l. During 30 to 400 days 1574 repeated blood samples were collected, with a median of 16 (IQR 15 to 17) for each patient. HsTnT above 14 ng/l (upper limit of normal) was observed in 26% of samples (in 49% of patients). The level of 50 ng/l was exceeded in 10 (0.6%) samples only. The within-patient variability explained 21% of total variation, and was thus much smaller than the between-patient variability (figure). The mean in hsTnT between 30 and 400 days was -1.4 ng/l.

Conclusions: High sensitivity troponin T (hs-TnT) is a sensitive biomarker used to diagnose acute myocardial infarction (AMI), with recent evidence suggesting it outperforms conventional TnT as a prognostic marker. Peak and time point conventional TnT levels (48 and 72 hours), are known prognostic markers. We sought to evaluate the relationship between hs-TnT levels with known adverse prognostic markers on cardiac magnetic resonance imaging (CMRI).

Methods: 90 consecutive patients with first presentation STEMI, undergoing PCI, were prospectively enrolled. Serial hs-TnT measurements were performed to determine peak, 48 hour and 72 hour levels. CMRI was performed at 5±3 days (early) and 14±1 days (follow-up) post STEMI. Left ventricular ejection fraction (LVEF) and mass were determined on cine MRI images by standard techniques. LV infarct size was determined by planimetry (mean±SD ROI) for core scar and 3-SD for border zone (BZ) scar on delayed gadolinium enhancement images.

Results: The study cohort (90% males, mean age 56±10 years), comprised of 13 (14%) who were diabetic and 49 (54%) who presented with an anterior STEMI. Peak, 48 hour and 72 hour hs-TnT levels negatively correlated with early and follow-up LVEF. All hs-TnT level parameters positively correlated with early and LV infarct size. Hs-TnT levels additionally correlated positively with both early and follow-up LV scar border zones. Utilizing a ROC curve analysis, 72 hr hs TnT >3,500 ng/l had a sensitivity 77% and specificity 84% in identifying patients with a follow-up LVEF <40%.

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Peak hs-TnT level</th>
<th>48hr hs-TnT level</th>
<th>72hr hs-TnT level</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF – early (%)</td>
<td>50 ± 10</td>
<td>r=−0.54</td>
<td>r=−0.52</td>
<td>r=−0.58</td>
</tr>
<tr>
<td>LV scar – early (%)</td>
<td>8.9 ± 5.6</td>
<td>r=0.58</td>
<td>r=0.63</td>
<td>r=0.65</td>
</tr>
<tr>
<td>LV scar – follow-up (%)</td>
<td>8.3 ± 5.5</td>
<td>r=0.63</td>
<td>r=0.67</td>
<td>r=0.68</td>
</tr>
<tr>
<td>LV scar BZ – early (%)</td>
<td>10.7 ± 5.2</td>
<td>r=0.52</td>
<td>r=0.57</td>
<td>r=0.58</td>
</tr>
<tr>
<td>LV scar BZ – follow-up (%)</td>
<td>14.5 ± 8.2</td>
<td>r=0.54</td>
<td>r=0.59</td>
<td>r=0.60</td>
</tr>
</tbody>
</table>

All p<0.001.

Conclusion: Peak, 48 hour and 72 hour hs-TnT levels are associated with adverse LV scar size and functional parameters during early LV remodeling post STEMI and predict adverse cardiac outcomes. High sensitivity hs-TnT levels correlated best with LV scar size and reduced LVEF. With long term follow up, these may be useful surrogate markers of adverse outcomes in STEMI.
Validation of two North-american risk scores for percutaneous coronary intervention in an European population of patients with acute coronary syndromes - comparison with GRACE risk score

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Introduction: GRACE risk score is an established tool for risk stratification in patients with Acute Coronary Syndromes (ACS). Recently, two new tools developed in the US for hospital mortality risk stratification in patients admitted to the Oct. The Oct coronary angioplasty have been published: the National Cardiovascular Data Registry (NCDR) and the Mayo Clinic Risk Score (MCRS). Both were validated in US populations. We sought to validate these score in an European population and compare it's predictive accuracy with the classical GRACE risk score.

Methods: Patients included in a single-centre ACS registry. Only patients submitted to coronary angioplasty were included in the analysis. For each case, a hospital mortality probability was given to each patient, who allowed building Receiver Operating Characteristics (ROC) curves and the Area Under Curve (AUC) was used to evaluate discriminative capacity of the model. Model accuracy was evaluated with a graphical representation of observed vs. expected mortality. We also analysed Net Reclassification Index (NRI) and Integrated Discrimination Improvement (IDI) for comparison of GRACE risk score with NCOR and MCRS scores.

Results: We included in the analysis 2,148 consecutive patients admitted with an ACS and submitted to coronary angioplasty. Mean age was 63.1±13.7 years, 74% males and 71% presented with ST-segment elevation acute myocardial infarction. Hospital mortality was 4.5%. In ROC curve analysis, GRACE score showed the best predictive power (AUC = 0.80, CI 0.73—0.86) compared with NCOR (0.67, 95% CI 0.63—0.70) and MCRS (0.65, 95% CI 0.61—0.69). GRACE score AUC was significantly higher compared with NCOR (p<0.0003) and MCRS (p<0.0003). In model calibration analysis, GRACE score showed the best predictive power, followed by NCOR and lower with MCRS, although we might consider it adequate. With GRACE score, patients were more correctly classified compared with MCRS (NRI 0.787, 95% CI 0.596—0.977, p<0.001; IDI 0.136, 95% CI 0.073—0.199, p<0.001) and NCOR (NRI 0.792, 95% CI 0.602—0.982, p<0.001; IDI 0.148, 95% CI 0.087—0.259, p<0.001).

Conclusion: NCDR and MCRS risk scores are useful for risk stratification of hospital mortality in an European population of patients with ACS submitted to coronary angioplasty. However, GRACE score has a better predictive power, and as such it should be the preferred score to be used.

Acute coronary syndrome in elderly patients - prognostic impact of revascularization

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Introduction: The proportion of patients with acute coronary syndrome (ACS) who are very old is increasing. These patients are a therapeutic challenge because they are rarely included in randomized clinical trials.

Aim: Determine clinical presentation, therapeutic approach and prognosis in a population of patients (Oct) with ACS.

Methods: Retrospective study of 2064 patients admitted for ACS in a coronary unit over a period of 4 years. 2 groups were defined according to age: younger (age <80 years, mean age = 60.9±11.4, n=1795) and Oct (age >80 years, mean age = 83.4±3.4, n=269).

Analysis of Oct according to therapeutic approach: percutaneous/surgical (n=177) vs medical (n=92). We determined the predictors of mortality in this group.

Results: In elderly patients there was a higher proportion of women (p<0.001) and comorbidities, such as chronic kidney disease (p<0.001), prior ACS (p<0.001) and previous stroke (p<0.001). Non ST Elevation Myocardial Infarction (NSTEMI) was the most common form of presentation in Oct (p=0.045). These patients had more multivessel disease (p=0.005), although they were less likely to receive evidence-based medical therapies or receive coronary angioplasty. However, GRACE score showed the best predictive power, followed by NCOR and lower with MCRS, although we might consider it adequate. With GRACE score, patients were more correctly classified compared with MCRS (NRI 0.787, 95% CI 0.596—0.977, p<0.001; IDI 0.136, 95% CI 0.073—0.199, p<0.001) and NCOR (NRI 0.792, 95% CI 0.602—0.982, p<0.001; IDI 0.148, 95% CI 0.087—0.259, p<0.001).

Conclusion: NCDR and MCRS risk scores are useful for risk stratification of hospital mortality in an European population of patients with ACS submitted to coronary angioplasty. However, GRACE score has a better predictive power, and as such it should be the preferred score to be used.

Incidence and implications of changes in left ventricular systolic function in a large regional ST-elevation myocardial infarction system

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Purpose: ST-elevation myocardial infarction (STEMI) is a common clinical event, often associated with detrimental effects on left ventricular systolic function (LVSF). However, limited real world data are available regarding which patients have further detriment or improvement in LVSF post-STEMI.

Methods: The “Level I MI” STEMI regional transfer system was initiated in 2003. Consecutive STEMI patients were followed prospectively for 5 years. The Level I database and electronic medical records were analyzed to see which patients had future improvement or detriment to LVSF post-STEMI.

Results: Over ten years (March 2003-March 2013), 3,720 STEMI patients were treated in the regional transfer system. Of the 3,573 patients that survived through discharge, 3,486 (97.6%) had a documented LVEF prior to discharge. Those 1,103 (30.9%) patients that had a follow-up echocardiogram or LVSF assessment beyond 40 days post-discharge were assessed to determine change in LVSF. One hundred twelve (18.7%) of the 599 patients with normal LVSF (>50%) at hospital discharge had decreased LVSF after 40 days post STEMI, including 6 patients (1%) who had decreased to <35%. Thirty-five (23.3%) of the 150 patients with severely reduced LVSF (<35%) had normalization of LVSF after 40 days, with 96 (62.7%) improving to >35%.

Conclusions: Left ventricular systolic function after STEMI changes in many patients regardless of discharge LVSF. Close follow-up of LVSF post-STEMI is warranted in all patients regardless of discharge LVSF.

The rs17228212 polymorphism in the intron of the SMAD3 gene is associated with 5-year mortality of patients with STE-elevation myocardial infarction

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Purpose: The rs17228212 (C/T) is a single nucleotide polymorphism located within the intron of the SMAD3 gene. It was shown to be associated with coronary artery disease and myocardial infarction in a genome-wide association study with cysteine (C) as a risk allele (1). The mechanism, however, remains unknown. The aim of our study was to investigate the association of the polymorphism with 5-year overall mortality in patients with STE-elevation myocardial infarction (STEMI) treated invasively.

Methods: We included in our registry consecutive patients with STEMI treated with primary PCI who survived 48 hours from hospital admission. Genotyping was performed with a TaqMan SNP Genotyping Assay using the ABI 7500 Real Time PCR System (Applied Biosystems). The analyzed end-point was total 5-year mortality.

Results: The study group comprised 641 patients (mean age 62.0±11.9 years; 25% of females, n=160; TIMI 3 obtained in 92.2%, n=591). The percentages of GC, CT and TT genotypes were 6.1% (n=39), 35.4% (n=227) and 58.5% (n=375), respectively. No significant differences were found between the genotypes in clinical characteristics. The 5-year total mortality was 16.4% (n=105). There died 23.1% (n=9) of CC homozygotes, 14.5% of heterozygotes (n=33) and 17.1% (n=63) of TT homozygotes (p=0.047, log-rank test).

Conclusions: The CC genotype of the rs17228212 polymorphism of the intron of the SMAD3 gene is associated with increased 5-year mortality in patients with STEMI.
Our data suggest that the C allele of rs1800795 on IL-6 gene pro-

**Conclusions:** [O.R=1.09, 95%C.I.(0.79-1.50), p=NS] or the risk for MI [O.R=1.07, 95%C.I.(0.71-1.58), p<0.001] (vs. GG homozygotes) and accelerates thus the atherosclerotic mechanisms in patients with already established CAD. (95% CI 1.67, 3.07)). In a stratified multivariate analysis (NSPR and SPR) adjusting for the Charlson Comorbidity Index (CCI) and including age at arrest (HR=1.28 (1.18, 1.39)), we observed that non-shockable primary rhythm (NSPR) was an independent predictor of mortality in patients with shockable primary rhythm treated with TH, stratified by their primary rhythm.

**Methods:** Consecutive unconscious survivors of OHCA in a Capital Region treated with TH between 2002-2011 were included. Utstein-based pre- and in-hospital data collection was performed. Data on co-morbidity was coded according to the Charlson Comorbidity Index (CCI).

**Results:** 665 unconscious survivors of OHCA treated with TH were included, 233 (35%) presented with NSPR. Significantly fewer patients were alive 30 days after OHCA with NSPR (28% vs. 62%, p<0.001), see figure. When adjusting for potential confounders, NSPR remained a significant predictor of mortality (HR=2.26 (95% CI 1.67, 3.07)). In a stratified multivariate analysis (NSPR and SPR) adjusting for known prognostic factors including sex, time to ROSC, witnessed arrest, bystander life support and cardiac etiology, age at arrest (HR=1.28 (1.18, 1.39) per five years) was an independent predictor of mortality in SPR patients only, p_interaction = 0.0018. However having any comorbidity (CCI>1) was an independent predictor in NSPR patients (HR=1.67 (1.08-2.59)) but not in SPR patients.

**Conclusion:** Unconscious survivors of OHCA with a non-shockable primary rhythm treated with hypothermia, carry a significantly higher mortality rate than patients presenting with shockable rhythm. Comorbidity was an independent predictor in patients presenting with non-shockable primary rhythm but not in shockable patients.
P1680 | BEDSIDE
Mortality in patients with extracorporeal life support is predicted by early progression of pulmonary edema - a prospective study
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Purpose: Extracorporeal life support (ECLS) serves as a powerful life-saving device in patients with cardiogenic shock refractory to conventional therapies. A potential shortcoming of veno-arterial (VA) ECLS support consists in its inability to provide adequate decompression of the failing left ventricle (LV) which may further enhance backward failure with pulmonary edema.

Hypothesis: Worse progression of pulmonary edema within the first 24 hours after initiation of ECLS may predict poor outcome.

Methods: Twenty-three consecutive patients with refractory cardiogenic shock ± resuscitation receiving femoro-femoral VA ECLS between March and December 2013 surviving initial 24 hours were included. Pulmonary edema was evaluated by blinded analysis of chest X-rays according to Halperin (Chest 1985) with scores between 0 (normal) and 390 (fulminant bilateral edema). Continuous variables were analyzed by Mann-Whitney test, categorical variables by Fisher’s exact test, survival analysis was computed by Kaplan-Meier techniques and log-rank test.

Results: Fourteen patients were diagnosed with ischemic cardiomyopathy, 6 patients with dilated cardiomyopathy, and one patient had a peripartum cardiomyopathy. Seventeen patients received cardiopulmonary resuscitation (67.5±1.4,1 min) prior to ECLS implantation. All patients initially presented with detectable pulmonary edema (Mean score 155.7±19.5) but a differential evolution of pulmonary edema in the disease course was observed: Eleven patients exhibited an increase of pulmonary edema scores within the first 24 hours (+32.3±20.76) while twelve patients presented stable or decreasing pulmonary opacification (-10.8±4.88). Increasing pulmonary edema scores predicted poor outcome (30 day mortality: Survival 25% ± 73%, p=0.01). Likewise, increasing pulmonary congestion was accompanied by reduced pulse pressure values (21±5.4 vs. 34±3.3; *) and a trend to larger LV diameters (66±5.9 vs. 60±2.6), potentially indicating progressive backward failure. Conversely, in patients receiving LV decompression by left ventricular assist device (LVAD) implantation (n=5) we observed resolution of pulmonary congestion (pre LVAD vs. day 5 post LVAD: 183±49.2 vs. 128±45.9; p=0.01).

Conclusion: Early progression of pulmonary edema within the first 24hr after ECLS implantation represents an indicator of poor prognosis. Potential therapeutic strategies may consist of early LV decompression.

P1681 | BEDSIDE
Increased mortality in women after out-of-hospital cardiac arrest is explained by an unfavorable pre-hospital risk profile
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Purpose: Out-of-hospital cardiac arrest (OHCA) is more frequent in men than in women, and current guidelines are based on research primarily performed in men. Previous observational studies suggest an unfavorable risk profile of OHCA in females, but the impact on long-term survival is not known.

Methods: From 2002-2011 consecutive patients with OHCA treated by the physician-based EMS-system in our city were included. Prehospital data according to Utstein-criteria, and data on in-hospital post-resuscitation care were collected.

Results: Women represented 31% (n=571) of resuscitated OHCA. Women were significantly older (68±15 vs. 63±14 years, p<0.001), more often had OHCA in a private setting (78% vs. 57%, p<0.001), less often had bystander CPR (47% vs. 59%, p<0.001), and primary rhythm was frequently non-shockable (63% vs. 42%, p<0.001), whereas time to ROSC was not longer (15 (9-23) minutes, p=0.4), compared with men. Cardiac etiology of the OHCA (73% vs. 84%, p<0.001) as well as acute coronary syndrome was less often seen in women (29% vs. 44%, p<0.001). Thirty-day mortality was 73% vs. 54% (p<0.001) corresponding to an unadjusted hazard ratio in women of 1.59 (95%CI: 1.38-1.83), p<0.001, Fig. 1A, but after adjusting for known prognostic factors, female gender was no longer associated with a worse prognosis (HR=1.03 (0.85-1.25), p=0.8), Fig. 1B.

Conclusion: Crude mortality after OHCA is higher in women than in men, which can be explained by differences in pre-hospital circumstances such as primary rhythm. Some of the pre-hospital risk factors in women with OHCA seem modifiable and may potentially contribute to improving survival in women.

P1682 | BEDSIDE
Association of seismic intensity after the great east japan earthquake and sudden out-of-hospital cardiac arrest
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Background: The increased occurrence of cardiovascular diseases after the Great East Japan was reported, but the nationwide effect and quantitative cut-off of seismic intensity was not examined. Our aim is to investigate whether the association between out-of-hospital cardiac arrest (OHCA) and seismic intensity after the Great East Japan Earthquake (magnitude 9.0 on March 11, 2011) is really exist.

Method and result: From 2008 to 2011, we conducted a study on OHCA using national database of cardiac arrest registry. Incidence rate ratio (IRR) of OHCA were analyzed by Poisson regression.

A total of 2308,290 adults with OHCA were included in this study; the trend is characterized by a marked peak between March 11 and March 31 in 2011 after the Great East Japan Earthquake compared to the same period in 2008-2010 all over Japan (IRR =1.72, 95%CI: 1.52-1.95). Compared to the incidence of March before the earthquake, the incidence on the day of Great Earthquake was doubled. (IRR=2.42, 95%CI: 1.59-3.59) The incidence rate of OHCA in 47 prefecture had a strong association with the seismic intensity in each prefecture (r=0.53, p=0.0003) (Fig. 1). Between the seismic intensity 4 and 5, the incidence of OHCA increased 27% (IRR=1.27, 95%CI: 1.00-1.62). Over the seismic intensity 4, which correspond to the peak ground acceleration greater than 4 m/s², the incidence rate of OHCA doubled compared with no earthquake period (IRR=2.02, 95%CI 4.52-2.68).

Conclusion: Large population based registry showed significant increase of OHCA nation-wide. The risk of cardiac arrest is highest in the area of seismic intensity over 6 and tend to increase in the area of seismic intensity 4 to 5. No significant increase of OHCA was observed under the seismic intensity four.

P1683 | BEDSIDE
Long-term outcome of patients with cardiogenic shock from acute myocardial infarction with and without intra-aortic balloon pump support

Purpose: Previous trials in patients with cardiogenic shock from STEMI undergoing PCI didn’t show a difference in mortality both at 30 days and 12 months between patients treated with and without IABP support. Clinical outcome at more extended follow-up has been reported less frequently. The aim of this study was to compare long-term outcome between patients with cardiogenic shock from STEMI treated with and without IABP.

Methods: A series of 544 consecutive patients admitted with cardiogenic shock from STEMI undergoing PCI were included between 2000-2012. The decision to use IABP support was made by the treating cardiologist.
crease in the occurrence of CPA, whereas inland patients had the bimodal peaks
compered the weekly occurrences in 2011 with those in the previous 3 years.
Methods: We enrolled patients with CPA of presumed cardiac origin by using the
intrinsic and common pathways of coagulation and rate of clinical bleeding
Conclusions: These results suggest that the increase in the occurrence of CPA
after the Earthquake was influenced by sex, age and residence area.

P1686 | BEDSIDE
Long-term survival and quality of life of patients submitted to
emergency coronary artery bypass grafting for post-infarction
cardiogenic shock
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Purpose: We have previously reported that the Great East Japan Earthquake increased
the occurrence of cardiopulmonary arrest (CPA), however, the details remain to be elucidated. In this study, we assessed the association between the Earthquake and the occurrence of CPA of presumed cardiac origin in more detail.
Methods: We enrolled patients with CPA of presumed cardiac origin using the
ambulance transport records database of Miyagi Prefecture, the center of the
disaster area, from February 11 to June 30 in each year of 2008-2011 (n=2,534)
and compared the weekly occurrences in 2011 with those in the previous 3 years.
Results: In the whole subjects, the weekly occurrence of CPA was significantly
increased with the bimodal peaks noted in the first 2 weeks after the Earthquake (March 11, 2011) and in the week just after the largest aftershock (April 7, 2011) compared with the previous 3 years. Sub-group analyses for sex and age (<75 or ≥ 75 years) showed that the occurrence of CPA was significantly increased soon after the Earthquake in all groups. However, male or younger patients did not show the second peak after the largest aftershock, whereas it was still noted in female and elderly patients (Figure). Furthermore, sub-group analysis for residence (seacoast vs. inland area) showed that seacoast patients had a sustained increase in the occurrence of CPA, whereas inland patients had the bimodal peaks (Fig. 1).

Figure 1

Conclusions: Patients with cardiogenic shock from STEMI undergoing PCI who
survive the first 30 days, have low annual mortality rates up to 10 years. There is no mortality difference associated with IABP support.

P1686 | BENCH
Targeted temperature management at 33°C compared to 36°C does not alter coagulations cascades and bleeding events after out-of-hospital cardiac arrest
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Purpose: Targeted temperature management after out-of-hospital cardiac arrest (OHCA) has been associated with increased bleeding events, due to temperature dependent impairment of coagulations cascades. We report the impact of a targeted temperature management at 33°C vs. 36°C on thrombocyte count, activity of the intrinsic and common pathways of coagulation and rate of clinical bleeding events.
Methods: Single centre study of 171 consecutive comatose OHCA patients assigned a targeted temperature management at 33°C (TTM33) vs. 36°C (TTM36) for 24 h as part of the TTM trial (NEJM 2013). We measured thrombocytes, Activated Partial Thromboplastin Time (APTT) and International Normalized Ratio (INR) at 0, 24, 48 and 72 h after cardiac arrest. Bleeding events were obtained from the TTM-database.
Results: Thrombocyte count decreased progressively from 228 ± 109 L-1 at base-line to 134 ± 109 L-1 at 72 h (p < 0.0001). APTT was longer at admission in ST-elevation myocardial infarction patients (58%) compared to others (194 vs. 65 seconds, p < 0.0001) due to pre-hospital treatment with heparin, but decreased to normal levels at 24-72 h. Emergency coronary angiography (<12 h) was performed in 75% and percutaneous coronary intervention (PCI) in 53% of patients, respectively. INR at baseline was 1.4 and remained unchanged throughout the observation period (p=0.23). Bleeding episodes were relatively rare, severe bleeding requiring blood transfusion (2%), gastrointestinal bleeding (4%) and bleeding from insertion sites (6%). All patients with severe bleeding underwent emergency PCI. There were no effects of TTM group allocation in any of the studied parameters, p > 0.2.
Conclusions: Coagulations cascades as well as clinical bleeding events are not influenced by targeted temperature management at 33°C compared to 36°C.

P1687 | BEDSIDE
Effect of coronary revascularisation on survival of patients with acute myocardial infarction and shock on ECMO
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Introduction: Management of post-myocardial infarction cardiogenic shock remains a matter of debate. Mechanical circulatory support as ECMO (extra corporeal membrane oxygenation) has shown encouraging results although evidence from randomized trials is lacking. Our goal was to evaluate whether the severity of coronary disease and myocardial revascularization may affect survival.
Methods: We performed an observational and single-center registry in a tertiary
Results: Half of the 106 included patients (mean age 52.7±14.0 years) pre-
sented a triple vessel disease. Revascularization by primary percutaneous in-
tervention (74.5%) was attempted in most of them. The rate of 30-day survival was 76.5% (P<0.05). However, the recent ISCHEM II trial demonstrated no benefit in short- and medium-term mortality with the use of IABP. It was our objective to evaluate in a real life population of patients included in a national registry of acute coronary syndromes, the impact of IABP in hospital mortality. Results: A total of 415 patients admitted for myocardial infarction (with and without ST segment elevation) in Killip class IV or who developed it in the first 24 hours after admission. All patients underwent coronary angiography in the first 24 hours. We evaluated demographic and baseline characteristics as well as treatment. The study objective was the occurrence of in-hospital mortality. Logistic regression analysis was performed to identify independent predictors of mortality. We also performed sub-group analysis. Results: From the 33.300 patients with myocardial infarction included in the registry, 29.330 (88%) Killip class IV in the first 24 hours and 6164 (43.6%) were submitted to coronary angiography and that was our study population. IABP was implanted in 19.8% of these patients. This group was younger and had higher admission heart rate. No differences were observed for other baseline characteristics or treatment except for more multivessel disease (68.5% vs. 72.5%, p<0.013) and more prevalence of left main disease (16.5% vs. 4.9%, p<0.001). There were 260 deaths, but similar were between groups (46.1% vs. 38.8%, p=0.132). There were also no significant differences in hospital complications. In sub-group analysis, there was no interaction with gender, age, diabetes or renal function. In patients with previous myocardial infarction and in patients without mechanical complications, the use of IABP was associated with higher mortality. In multivari-
ate analysis, the use of IABP was associated with higher risk of hospital mortality (OR 1.77, 95% CI 1.15-2.73, p=0.010). The other predictors were age, smoking and antithrombotic treatment.

Conclusions: In a real life population of patients with acute myocardial infarction, the use of IABP for the treatment of cardiogenic shock has no benefit in short-term prognosis.

ACUTE CORONARY SYNDROME – PROGNOSIS AND MANAGEMENT

P1689 | BEDSIDE
Role of intra-aortic balloon pump counterpulsation in the treatment of acute myocardial infarction complicated by cardiogenic shock: what are the real evidences from registries?

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International guidelines recommend the use of intra-aortic balloon pump (IABP) in the treatment of cardiogenic shock in the context of acute myocardial infarction as an off-label treatment. However, the recent ISCHEM-II trial demonstrated no benefit in short- and medium-term mortality with the use of IABP. It was our objective to evaluate in a real life population of patients included in a national registry of acute coronary syndromes, the impact of IABP in hospital mortality.

Methods: A total of 415 patients admitted for myocardial infarction (with and without ST segment elevation) in Killip class IV or who developed it in the first 24 hours after admission. All patients underwent coronary angiography in the first 24 hours. We evaluated demographic and baseline characteristics as well as treatment. The study objective was the occurrence of in-hospital mortality. Logistic regression analysis was performed to identify independent predictors of mortality. We also performed sub-group analysis. Results: From the 33.300 patients with myocardial infarction included in the registry, 29.330 (88%) Killip class IV in the first 24 hours and 6164 (43.6%) were submitted to coronary angiography and that was our study population. IABP was implanted in 19.8% of these patients. This group was younger and had higher admission heart rate. No differences were observed for other baseline characteristics or treatment except for more multivessel disease (68.5% vs. 72.5%, p<0.013) and more prevalence of left main disease (16.5% vs. 4.9%, p<0.001). There were 260 deaths, but similar were between groups (46.1% vs. 38.8%, p=0.132). There were also no significant differences in hospital complications. In sub-group analysis, there was no interaction with gender, age, diabetes or renal function. In patients with previous myocardial infarction and in patients without mechanical complications, the use of IABP was associated with higher mortality. In multivari-
ate analysis, the use of IABP was associated with higher risk of hospital mortality (OR 1.77, 95% CI 1.15-2.73, p=0.010). The other predictors were age, smoking and antithrombotic treatment.

Conclusions: In a real life population of patients with acute myocardial infarction, the use of IABP for the treatment of cardiogenic shock has no benefit in short-term prognosis.

P1690 | BEDSIDE
The variants rs243327, rs243330, rs33977706 and rs33932899 of the SOCS1 gene polymorphisms were analyzed by 5’ exonsucase TaqMan geno-
yping assays in a group of 447 patients with ACS and 622 healthy controls.

Results: 3969 C-T, 1566 G-A, 820 G-T and +1125 G-C single nucleotide polymorphisms showed that the “CT” genotype of the -3969 C-T SNP was signifi-
cantly associated with an increased risk of ACS as compared to controls un-
der heterozygous model (OR=1.47, 95% CI: 1.06-1.98, P=0.001). On the other side, the “AG” genotype of the -1566 G/A SNP was significantly associated with increased risk of ACS when compared to controls under dominant and het-
erozygous models (OR=1.65, 95% CI: 1.11-2.38, P=0.01, 1.55, 95% CI: 1.04-2.21, 1.61, 95% CI: 1.02-2.56, respectively). Moreover, the “GT” or “GG” geno-
types of the -820 T/G SNP was significantly associated with increased risk of ACS as compared to controls under dominant, and heterozygous mod-
els (OR=1.59, 95% CI: 1.14-2.28, P=0.013, 1.48, 95% CI: 1.04-2.10, 1.51, 95% CI: 1.00-2.26, respectively). The CG type of the +1125 G/C SNP was significantly associated with increased risk of ACS when compared to controls under dominant and heterozygous models (OR=1.54, 95% CI: 1.08-2.21, P=0.05, 1.58, 95% CI: 1.12-2.27, P=0.012, respectively). Models, were adjusted for gender, age, body index mass, dyslipidemia, alcohol consumption, and smoking.

Conclusion: In summary, our data suggest that the variants rs243327, rs243330, rs33977706 and rs33932899 of the SOCS1 gene play an important role as sus-
cceptibility marker for developing ACS.

P1691 | BENCH
Secreted wingless (Wnt) antagonists and risk prediction in acute coronary syndrome (ACS) a PLATO biomarker substudy

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Background: Recent studies suggest that the Wnt pathway may be implicated in vascular remodeling and atherosclerosis. To gain further insight into the role of Wnt-related mediators in atherosclerotic disorders, we investigated the prognos-
tic value of the Wnt pathway modulators serum secreted frizzled related protein 3 (sFRP-3) and Dickkopf-1 (DKK-1) for 1-year outcome in patients with acute coro-

nary syndromes (ACS).

Methods: sFRP-3 and DKK-1 levels were determined in serum collected at ran-
domization to ticagrelor or clopidogrel in 4201 patients with ACS in the PLATO (PLAto inhibition in patients with acute coronary Syndromes) study. Baseline characteristics by Chi-
square test (categorical variables) or Kruskal Wallis test (continuous variables), and occurrence of the primary outcome, a composite of cardiovascular death, non-fatal myocardial infarction, or stroke (n=363), by Cox proportional hazards models were compared between groups stratified by quartiles of the respective biomarker.

Results: The median (interquartile range) of DKK-1 was 0.6 (0.2 – 1.3) and of sFRP-3 13.0 (3.3 – 36.8). Higher frequencies of hypertension, diabetes mellitus, angina, previous MI and heart failure and higher levels of CRP and NT-proBNP were associated with increasing quartiles of DKK-1 (p<0.001 for all, except diabe-
tes p=0.01), and opposite trends were seen for sFRP-3 with the lowest risk factor

zyances concerning outcomes in ACS. This pattern indicates a complex role for the Wnt pathways in clinical atherosclerosis involving regulation of soluble Wnt mediators.

Conclusions: Higher DKK-1 was less often seen in STEMI, while this trend was opposite for sFRP-3. There was a significant inverted U shaped prognostic pattern of Wnt antagonists concerning outcomes in ACS. This pattern indicates a complex role for the Wnt pathways in clinical atherosclerosis involving regulation of soluble Wnt mediators.
**Results:** In our study cohort (age 66±12 years, LVEF 55±12%), cardiovascular events observed in 29 patients (6.8%). In Kaplan-Meier analysis, patients with high levels of GDF-15 (≧1312.5 ng/L) showed worse prognosis than patients with low levels of GDF-15 (<1312.5 ng/L) (p=0.001). Patients with high levels of hs-CRP ST2, and IL-6 did not show the difference as to cardiovascular events. GDF-15 was associated with the risk of cardiovascular events after adjustment for age and LVEF (hazard ratio: 1.86, 95% confidence interval: 1.04 to 3.33; p=0.037). GDF-15 provided an incremental predictive value for cardiovascular events over clinical features (incremental in global χ²=14.89, p=0.001).

**Conclusions:** In patients with AMI, high levels of GDF-15 were associated with higher incidence of cardiovascular events after PCI although hs-CRP ST2, and IL-6 failed to show the difference. GDF-15 provided incremental prognostic value to clinical features.

**Methods:** We enrolled 429 patients with AMI, who were measured with high-sensitivity C reactive protein (hs-CRP), growth differentiation factor-15 (GDF-15), interleukin-1 receptor family member called ST2 (ST2), and interleukin-6 (IL-6) after successful percutaneous coronary intervention (PCI). Patients were prospectively tracked for 2 years. The relation of biomarkers to cardiovascular events was also assessed.

**Results:**

1. **Kaplan-Meier curves according to GDF-15.**

2. **P1694 | BEDSIDE**

Pentraxin 3 (PTX3) predict adverse outcome in acute coronary syndromes - a PLATO biomarker substudy


**Purpose:** PTX3 is expressed by the major cell types involved in atherosclerosis in response to inflammatory stimuli and may be regarded as a marker of local vascular inflammatory response. In the current study we investigated the association between levels of PTX3 and 1-year outcomes in patients with acute coronary syndromes (ACS).

**Methods:** PTX3 was determined in plasma sampled at randomization to ticagrelor or clopidogrel in 4191 patients with ACS enrolled in the PLATO (Platelet Inhibition and Patient Outcomes) trial. Patients were categorized based on quartiles of PTX3 levels and compared with respect to baseline characteristics (Chi-square or Kruskal Wallis tests for categorical and continuous variables, respectively), and to the primary composite endpoint of cardiovascular death, myocardial infarction (MI), or stroke (Cox proportional hazards models).

**Results:** The median (interquartile range) range of PTX3 was 1.9 ng/mL (1.2 – 3.0 ng/mL). Higher PTX3 levels were associated with higher age, higher number of female gender, lower Body Mass Index, less smokers, higher frequency of chronic kidney disease (p=0.0001 for all), and lower occurrence of ST-elevation MI (p=0.0071). Higher PTX3 levels were also associated with both TIMI and GRACE risk scores, and with higher Troponin I, NT-proBNP, and C-reactive Protein levels (p=0.0001 for all). No association was found with presence of diabetes mellitus or past medical history (e.g. coronary or peripheral artery disease, congestive heart failure, or stroke). Higher rates of the primary endpoint were found in the two upper PTX3 quartiles (Q3 and Q4: 10.5 and 11.7%)year; HR [95%CI]: 1.47 [1.08-1.98] and 1.64 [1.22-2.20], respectively) in comparison to the lowest quartile (7.1%year), p=0.0006. There was no significant interaction between PTX3 levels and the effects of randomized treatment.

**Conclusions:** In patients with ACS, PTX3 levels are related to age and markers of myocardial damage and dysfunction, kidney dysfunction and inflammatory activity. High admission levels of PTX3 are associated with adverse clinical outcomes up to 12 months after ACS. The benefits of ticagrelor versus clopidogrel are independent of the PTX3 levels.

**P1695 | BEDSIDE**

Impact of fixed atherosclerotic coronary lesion in patients with coronary artery spasm on 3-year clinical outcomes

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**Background:** Coronary artery spasm (CAS) and fixed atherosclerotic coronary lesion (FCL) are both known to be a major cause of myocardial ischemia. However, their association and impact on long-term clinical outcomes are largely unknown.

**Methods:** A total of 2,797 consecutive pts without significant coronary artery disease who underwent Ach provocation test were enrolled between November 2004 and October 2010. Pts were divided into two groups according to the existence of FCL (FCL group: n=765, non-FCL group: n=1,042). We evaluated the impact of FCL in patients (pts) with CAS on 3-year clinical outcomes.

**Results:** At baseline, pts with FCL had a higher incidence of elderly, male, hypertension, diabetes and dyslipidemia than pts without FCL. During Ach provocation test, the FCL group showed more severe narrowing than the non-FCL group, whereas the non-FCL group had higher incidence of myocardial bridge and baseline spasm. The FCL group had a higher incidence of major adverse cardiovascular & cerebrovascular events (MACCE) including all-cause mortality, myocardial infarction, coronary revascularization and cerebrovascular accidents (1.3% vs. 0.2%; p=0.013) at 3 years. However, there was no significant difference between the two groups after multivariate analysis (HR; 3.85, 95%CI; 0.8-18.4, p=0.081) and after propensity score matching analysis (HR; 5.13, 95%CI; 0.57-45.8, p=0.143).

**Table:** 3-year cumulative clinical outcomes

**Conclusion:** In this study, the presence of FCL in vasospastic angina pts was not associated with adverse 3-year clinical outcomes as compared with vasospastic angina pts without FCL.

**P1696 | BEDSIDE**

Can the severity of initial presentation of coronary spasm predict the prognosis?


**Background:** There are many proven risk factors to estimate the prognosis of atherosclerotic coronary disease. On the contrary to this, outcome prediction of coronary spasm is challenging. This study aimed to identify the impact of initial presentation of coronary spasm on the prognosis.

**Methods:** From 2001 to 2012, among ergonovine-test proven 271 consecutive coronary spasm patients, 221 patients (mean age 57±9.7, 178 male) were retrospectively enrolled, excluding the patients with previous percutaneous coronary intervention or angiographically more than 50% coronary stenoses. We divided the cohort with two groups depending on whether the initial presentation of the patients was angina or myocardial infarction (MI)/syncpe/aborted cardiac arrest. Primary endpoint was composite of emergency room visit for anginal symptom, nonfatal MI, and cardiac arrest. Secondary endpoint was composite of non-fatal MI and cardiac arrest.

**Results:** Among 221 patients, angina was an initial presentation in 163 patients, MI in 45 patients, syncope in 9 patients and cardiac arrest in 4 patients. Mean follow-up duration was 3.2 years. We assigned angina patients as “group A” and non-fatal MI/syncope/aborted cardiac arrest patients as “group B”. Patients in group A were older than group B (56±9.7 vs. 54±9.0, p=0.011). There were no intergroup differences in baseline characteristics of body mass index, left ventricular ejection fraction, N-terminal pro-B-type natriuretic peptide, serum monocyte count, lipid profiles, hypertension, diabetes, smoking, discharge medications and hemodynamic unstable events during ergonovine test. For primary endpoint, Group B showed worse outcome than group A in Kaplan-Meier survival analysis (34.5% vs. 17.2%, log rank p=0.006). For secondary endpoint, group B also showed significantly worse outcome than group A in Kaplan-Meier survival analysis (17.2% vs. 3.7%, log rank p<0.001).

**Conclusions:** Severity of initial presentation could be a predictor for long-term outcome of patients with coronary spasm.
### P1696 | BEDSIDE

**Prognostic implications of the absence of chest pain in patients with high troponin levels in emergency department**

G.C. Cediel, A. Carrasque, C. Boque, R. Sanchez, A. Bardaji, Joan XXIII University Hospital, Tarragona, Spain

**Introduction:** A positive troponin (TnI) is an independent predictor of adverse outcomes. TnI analysis is often done in the absence of chest pain. The objective of our study was to establish the prognostic value of a high TnI in the absence of chest pain: respective of the final diagnosis.

**Methods:** Retrospective analysis of adult patients admitted in our emergency department in the first semester of 2012 and who had at least a determination of TnI. Demographic, clinical data and final diagnosis were obtained from the medical records.

**Results:** In-hospital and 1-year survival was analyzed. Patients were categorized into four groups for analysis: chest pain and normal TnI; chest pain and raised TnI; without chest pain and normal TnI; and without chest pain and raised TnI. Were observed significant differences in prevalence of systemic arteriographic when p<0.05.

**Conclusions:** In patients with acute coronary syndromes intervention in culprit vessel only showed be safe and similar prognostics were observed in long term follow-up in patients with or without significant residual coronary occlusion.

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### P1698 | BEDSIDE

**Minimalist immediate mechanical intervention (MIMI) strategy for STEMI aims to restore normal anterograde flow in the culprit artery and to defer potential stent implantation after a few days of optimal antithrombotic therapy. The goal of the present study was to assess the applicability of this strategy and its impact on STEMI treatment modalities in daily practice.**

**Methods:** All consecutive patients admitted for acute STEMI in our institution between June 2010 and June 2013 were included. All patients underwent first a de-recanalization of the culprit lesion (manual thrombectomy and/or balloon predilation, under double antiplatelet therapy + heparin) in order to restore anterograde flow in the culprit vessel. The MIMI strategy was considered when an optimal reruptor (angiographic TIMI grade flow >2 + ST segment elevation regression ≥50% is obtained. The MIMI patients were subjected to a subsequent angiography control after a few days of optimal antithrombotic therapy with additional angioplasty and stent implantation if required. The other patients were included in the control/standard therapy group.

**Results:** Major adverse cardiovascular events (MACE: cardiac death+stent thrombosis+ recurrent myocardial infarction+ target vessel revascularization) were subsequently recorded >2.4% after hospital discharge.

**Conclusions:** The absence of chest pain in patients with a TnI level above the reference limit is an independent predictor of mortality.

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### P1697 | BEDSIDE

**Long term prognosis of acute coronary syndromes submitted to angioplasty in culprit vessel only-Comparison between complete treatment versus residual lesion**

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**Purpose:** To analyse the demographic data and outcomes of patients with acute coronary syndromes submitted to percutaneous coronary intervention in culprit vessel only comparing patients with residual nonculprit coronary lesions higher than 70% occluded (group I) versus patients without significant residual nonculprit coronary lesions (group II).

**Methods:** This was a prospective data bank analysis study with 580 patients (284 in the group I and 296 in the group II) with acute coronary syndromes included between May 2,010 and May 2,013. The following data were obtained: age, sex, diabetes, systemic arterial hypertension, smoke, dyslipidemia, familial history of preocose coronary artery disease, previous coronary artery disease (percutaneous coronary intervention or coronary artery bypass graft), hemoglobin, creatinine, higher troponin, left ventricle ejection fraction, medication used at hospital and coronary definitive treatment. The primary endpoint was combined events (death, non-fatal unstable angina or myocardial infarction, repeated revascularization and heart failure). Comparison between groups was made by Anova and Q-square. Long term results were studied using Kaplan-meier curves with median follow-up of 9.86 months and was considered significant when p<0.05.

**Results:** The median age was 63 years versus 62 years in the groups I and II, respectively. Were observed significant differences in prevalence of systemic arterial hypertension (74.4% x 81.2%, p<0.04), smoke (41.9% x 35.1%, p=0.009), familial history of preocose coronary artery disease (15.0% x 8.8%, p<0.02), use of B-blocker (80% x 65.6%, p<0.001), use of enoxaparin (87.5% x 73.2%, p<0.001), use of angiotensin converting enzyme inhibitor (68.1% x 56.3%, p<0.006), creatinine (1.15 x 1.35 mg/dl, p=0.03) and higher troponin (18.3 x 8.04 ng/mL, p=0.005), respectively between groups I and II. Long term follow-up showed similar results between groups I and II in combined events (46.1% x 53.9%, p<0.07).

**Conclusions:** In patients with acute coronary syndromes intervention in culprit vessel only showed be safe and similar prognostics were observed in long term follow-up in patients with or without significant residual coronary occlusion.

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### P1699 | BEDSIDE

**Efficacy of everolimus-eluting stent implantation in patients with small coronary arteries. Outcomes of 2-year clinical follow-up**

H.Y. Yano1, M.I. Ishikawa1, S.H. Horinaka2, T.I. Ishimitsu2, 1 Nasu Redcross Hospital, Tochigi, Japan; 2 Dokkyo Medical University, Tochigi, Japan

**Background:** Previous studies have demonstrated that patients with small coronary artery lesions (SCAL) are at increased risk for late cardiac events after percutaneous coronary intervention (PCI). It remains uncertain whether second-generation drug-eluting stents have an advantage first-generation drug-eluting stents (DES) in patients with SCAL. This study aimed to evaluate the long-term efficacy of everolimus-eluting stent (EES) and sirolimus-eluting stents (SES) on SCAL.

**Methods and results:** Consecutive 360 patients with 405 SCAL, who were treated with EES (157 patients, 185 lesions) and SES (203 patients, 220 lesions) were enrolled. SCAL was defined the lesions with reference vessel diameter (RVD) <2.5 mm. Within ten months angiographic follow-up results and 3-year clinical follow-up outcomes were compared between EES and SES groups. The proportion of diabetes was higher and the stent length was longer (23.0±7.0 vs. 20.1±6.8, p<0.05) in EES group than in SES group. Initial success rate was similar in both groups. There was no difference in 3-year %binary restenosis, TLR (2.1vs. 4.7%), and MACE (3.8% vs 7.7%) rates between 2 groups. This similar major adverse cardiovascular events rate remained after adjustment. However, the rate of stent thrombosis was 0% in the EES group and 1.8% in the SES group (p<0.04).

**Conclusions:** EES demonstrated favorable clinical outcomes to those of SES in SCAL patients. The absence of stent thrombosis among patients treated with EES suggests a good safety profile for this second-generation drug-eluting stent, which should be carefully studied in a larger series of patients with SCAL.
STABLE CORONARY ARTERY DISEASE: INVASIVE AND MEDICAL STRATEGIES

P1701 | BEDSIDE
Does percutaneous coronary intervention reset disadvantage in long-term outcome in patients with functionally significant stenosis?

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Background: In patients with stable coronary artery disease, fractional flow reserve (FFR) guided percutaneous coronary intervention (PCI) for functional significant stenosis improves clinical outcome as compared with medical therapy alone. However, it is not clear whether PCI can reset disadvantage in long-term outcome to the same level of patients without significant stenosis. To evaluate the extent of therapeutic efficacy of PCI, we compared the long-term outcome between patients treated with PCI and patients without functionally significant stenosis.

Methods: Stable angina patients with visually stenotic lesions (<50% stenosis) were assessed by FFR measurements. Patients with at least one functionally significant stenosis (FFR<0.8) were treated by drug-eluting stents implantation (PCI group). Patients without functionally significant received best available medical treatment (Deferral group). Any death, myocardial infarction, stroke, and any revascularization were considered major adverse cardiac events (MACE). The incidence of MACE was compared between both groups.

Results: A total of 154 patients were enrolled in this study (114 in PCI group and 40 in Deferral group). Mean follow-up period was 577 days. The incidence of MACE was similar between the PCI and Deferral group during first 6 months (p=0.18). However, beyond 6 months follow-up, PCI group had significantly higher incidence of MACE as compared to Deferral group (33.3% vs. 3.13%; p=0.01).

Conclusion: Although short-term outcome is similar, the incidence of MACE increases between 6 months and 3 years in patients with drug-eluting stents treatment as compared to deferral patients.

P1702 | BEDSIDE
Reduced benefit of final kissing balloon inflation after single stenting to bifurcations lesions in patients with diabetes: Insight from the optical coherence tomography sub-study of J-REVERSE trial

T. Shinke1, Y. Murasato2, Y. Kinoshita3, K. Fujii4, Y. Takeda4, H. Otake4, H. Hariki2, H. Kinutani4, H. Takahashi4, K. Hirata1,1 Kobe University, Division of Cardiovascular Medicine, Kobe, Japan; 2Shin Yukuhashi Hospital, Department of Cardiovascular Medicine, Yukuhashi, Japan; 3Toyohashi Heart Center, Department of Cardiovascular Medicine, Toyohashi, Japan; 4Hyogo Medical College, Department of Cardiovascular Medicine, Nishinomiya, Japan; 5Rinku Medical Center, Department of Cardiovascular Medicine, Izumisano, Japan

Background: Diabetes mellitus (DM) and bifurcation lesions are still leading causes of unfavorable outcomes after drug-eluting stent implantation. The impact of DM on vessel reaction to final kissing inflation (FKI) following single stenting between everolimus- (EES) and paclitaxel-eluting stents (PES) in patients with small coronary artery diseases. Inclusion criteria were 1) Lesions <2.5mm in diameter, 2) lesion length <28mm. The primary endpoint is clinical driven target lesion revascularization (TLR) rate at 2 year.

Results: In EES group, a non-significant trend toward rate of major adverse cardiac events, however, 2 year TLR rate was significantly lower than PES group (Table).

Conclusion: EES showed better clinical results for treatment of small coronary artery diseases.

P1703 | BEDSIDE
Two year follow-up results of everolimus and paclitaxel-eluting stents for small coronary artery diseases: final results of PLUM and SACRA registries

K. Nasu1, Y. Okawa2, S. Shira3, H. Abe4, H. Hozawa5, S. Tohara6, M. Kadotani7, A. Okuma7, Y. Takeda7, R. Goto7 on behalf of PLUM and SACRA investigators. 1Toyohashi Heart Center, Toyohashi, Japan; 2The Cardiovascular Institute Hospital, Tokyo, Japan; 3Kokura Memorial Hospital, Department of Cardiology, Kitakyushu, Japan; 4Matsumoto Kyoritsu Hospital, Cardiovascular Center, Matsumoto, Japan; 5Ayase Heart Hospital, Cardiovascular Medicine, Kasukabe, Japan; 6Kasukabe Chuo General Hospital, Kasukabe, Japan; 7Kakogawa East City Hospital, Kakogawa, Japan; 8Takurabashi-Watanabe Hospital, Osaka, Japan; 9Rinku General Medical Center, Izumisano, Japan; 10SHIWA General Hospital, Kasukabe, Japan

Purpose: Percutaneous coronary interventions involving small coronary vessels represent a true challenge because of the increased risk of restenosis and adverse outcomes. The aim of this study is to evaluate the 2-year clinical results following small coronary stenting between everolimus- (EES) and paclitaxel-eluting stents (PES).

Methods: PLUM (PROMUS/Xience V Everolimus-ELUting Coronary Stent for small coronary artery disease: 264 patients with 279 lesions) and SACRA (SmAll Coronary Arty treated by TAXUS Liberté: 245 patients with 258 lesions) registries are prospective, multicenter registries to assess the efficacy of single EES and PES in patients with small coronary artery diseases. Inclusion criteria were 1) Lesions <75% diameter stenosis in vessels <2.5mm in diameter, 2) lesion length <28mm. The primary endpoint is clinical driven target lesion revascularization (TLR) rate at 2 year.

Results: In EES group, a non-significant trend toward rate of major adverse cardiac events, however, 2 year TLR rate was significantly lower than PES group (Table).

Two-year clinical results

<table>
<thead>
<tr>
<th>Event</th>
<th>EES</th>
<th>PES</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>264</td>
<td>245</td>
<td></td>
</tr>
<tr>
<td>Lesions, n (%)</td>
<td>279</td>
<td>258</td>
<td></td>
</tr>
<tr>
<td>Cardiac death at one year, n (%)</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Cardiac death at two year, n (%)</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction at one year, n (%)</td>
<td>2 (0.8%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction at two year, n (%)</td>
<td>2 (0.8%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>TLR at one year, n (%)</td>
<td>11 (4.2%)</td>
<td>25 (10.6%)</td>
<td>0.009</td>
</tr>
<tr>
<td>TLR at two year, n (%)</td>
<td>12 (4.5%)</td>
<td>26 (10.6%)</td>
<td>0.01</td>
</tr>
<tr>
<td>TVR at one year, n (%)</td>
<td>20 (7.6%)</td>
<td>32 (13.1%)</td>
<td>0.06</td>
</tr>
<tr>
<td>TVR at two year, n (%)</td>
<td>21 (8.0%)</td>
<td>35 (13.9%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Any MACE at one year, n (%)</td>
<td>22 (8.3%)</td>
<td>33 (13.5%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Any MACE at two year, n (%)</td>
<td>23 (8.7%)</td>
<td>35 (14.3%)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Conclusion: These results show better clinical outcomes for treatment of small coronary artery diseases.

P1704 | BEDSIDE
Outcome after drug-eluting stents for cardiac allograft vasculopathy


Purpose: Cardiac allograft vasculopathy (CAV) constitutes a primary cause of
death after heart transplantation. Bare metal stents (BMS) have been used for revascularization, but they are associated with a high-risk of restenosis. Limited data have shown favourable results with percutaneous coronary interventions (PCI) using drug-eluting stents (DES) in this specific population. Our study focuses on intrastent restenosis (ISR) for DES in CAV, on new revascularisation and methods.

Methods: 97 consecutive heart transplant recipients with successful PCI were treated with DES (n=106) and BMS (n=25). They were prospectively followed-up at one year after PCI. An angiographic lesion-based analysis at 12-month follow-up and a patient-based survival analysis were performed.

Results: The lesion-based analysis within 12 months after PCI showed an ISR rate with BMS of 12% and an ISR rate with DES of 3.8%. The target lesion revascularization rate was 8% for BMS and 2.8% for DES. However, the target vessel revascularization rate was higher in DES (16.5%) compared with bare-metal stents. It remains uncertain whether second-generation drug-eluting stents have an advantage over bare-metal stents (BMS) in patients with LCAL. This study aimed to evaluate the long-term efficacy of everolimus-eluting stent (EES) and BMS on large coronary artery lesions.

Methods and results: Consecutive 394 patients with 441 LCAL, who were treated with EES (191 patients, 214 lesions) and BMS (203 patients, 227 lesions) were enrolled. LCAL was defined as the lesions with the use of stent size of ≥3.5mm. Within ten months angiographic follow-up results and 2-year clinical follow-up were compared with bare-metal stents. It remains uncertain whether second-generation drug-eluting stents have an advantage over bare-metal stents (BMS) in patients with LCAL. This study aimed to evaluate the long-term efficacy of everolimus-eluting stent (EES) and BMS on large coronary artery lesions.

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### Stable coronary artery disease: invasive and medical strategies / Remote ischemic preconditioning, thrombectomy and no reflow

#### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Basal CFR</th>
<th>One month CFR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ivaludrine</td>
<td>2.67±0.55</td>
<td>3.52±0.64</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>2.72±0.55</td>
<td>3.35±0.70</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>p</td>
<td>ns</td>
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<td></td>
</tr>
</tbody>
</table>

CFR: coronary flow reserve.

#### P1710 | BEDSIDE

Comparison of the efficacy and tolerability of Ivaludrine vs ranolazine vs standard medical therapy in patients of chronic stable angina pectoris despite coronary percutaneous revascularization

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**Background:** Despite treatment with conventional agents plus complete coronary revascularization, many patients remain symptomatic. Therefore, new drugs, as Ivaludrine and Ranolazine, able to reduce ischemic episodes. Objective was to evaluate the effects of Ivaludrine and Ranolazine plus standard therapy vs only standard therapy in terms of an increased exercise tolerability and a decreased incidence of angina episodes at 30 days. Secondary end-point was to evaluate, at 6-12 months clinical follow-up, the incidence of weekly angina episodes and re-hospitalization.

**Methods:** One hundred thirty-five consecutive patients who underwent to percutaneous coronary intervention plus stent implantation and met inclusion criteria were randomized in three different arms to receive Ivaludrine (5mg twice daily)+standard therapy, Ranolazine (375mg twice daily)+ standard therapy or conventional anti-ischemic therapy alone. At 30 days all patients were submitted to treadmill exercise test (ETT) and symptoms, ECG variations and maximal time exercise were recorded. Clinical follow-up was performed at 30 days, 6 and 12 months.

**Results:** Patients were randomized in three arms in a 1:1:1 ratio: Ivaludrine Group 45 pts (IG), Ranolazine Group 45 pts (RG) and Control Group 45 pts (CG). No baseline clinical and therapies differences were found between groups. At 30±5 days ETT was performed in all patients. During the ETT only 11.1% IG and RG did not exceed the threshold of the six minutes vs 28.8% GC (p=0.03). 5 patients in IG and in RG developed angina in the first 6 minutes of exercise (CG vs IG vs RG p=0.03). At 30 days, 24.4% developed weekly angina during daily moderate exercises in CG vs 4.5% in IG (p=0.007), and 8.8% in RG (p=0.04). At 6 months follow-up showed significant difference in angina onset between RG (5 pts) vs IG (7 pts) vs CG (19 pts) (p=0.005 CG vs IG and p=0.008 CG vs RG). At 12 months follow-up 6 weekly anginas was ever greater in CG (42.2%) compared with RG (p=0.002) and (p=0.005). Re-hospitalization, for angina worsening, was 12 months was necessary in only 2 pts treated with Ivaludrine vs 9 pts in CG and 5 pts in RG (CG vs IG p=0.02).

**Conclusions:** The addition of Ivaludrine/Ranolazine with standard anti-ischemic therapy in patients with complete revascularization produce an increased efficacy and safety in terms of a significant improvement of exercise tolerability, a decrease daily angina episodes and re-hospitalization angina guided.

#### P1714 | BEDSIDE

Effect of rosuvastatin treatment on skin microvascular function in patients with coronary artery diseases assessed by laser Doppler flowmetry


**Purpose:** The involvement of microvascular bed in atherosclerosis in absence of arterial hypertension is not well established. Our aim was to investigate the impact of lipid lowering therapy by Rosuvastatin on skin microvascular function as the model of myocardial microcirculation in patients with coronary artery diseases (CAD).

**Methods:** 14 pts with coronary artery disease (9 male, 5 female, mean age 57.6±8.1), without diabetes, hypertension, heart failure, never treated with lipid-lowering medication were examined before and after 12 weeks of Rosuvastatin treatment (10 mg/day). All pts had exertional angina CCS grade I-III and finding of severe stenoses in their coronary angiography. Antianginal therapy by β-blockers (bisoprol 5mg/day) and nitrates (mononitrates 40 mg/day) was not discontinued. Skin microvascular function was assessed by laser Doppler flowmetry at rest, with the constrictor (respiratory and venous occlusion) and dilator (heating, electrostimulation and arterial occlusion) tests on the ulnar part of the right forearm. Amplitude–frequency wavelet analysis of blood flow oscillations was performed. Time-averaged vasomotion amplitude was assessed using maximum values (Amax) in the corresponding frequency band for endothelial (AE), neurogenic (An), myogenic (Am), venular (Av) and cardiac (Ac) sections of blood flow modulation. Values of the tissue perfusion level (M) and the amplitude modulation mechanisms evaluated in AU.

**Results:** Rosuvastatin treatment resulted in a decrease of total cholesterol from 6.32±1.109 to 4.9±1.27 mmol/l, LDL-cholesterol from 4.3±0.8 to 2.9±1.02 mmol/l (p=0.002). Against this background, there is an increase with a tendency to reliability level of M with 3.92 to 5.17 AU (+0.065), a significant increase in the amplitude vasomotion of Ac with 0.265 to 0.405 AU (-0.01), An with 0.246 to 0.403 AU (-0.003) and Am with 0.199 to 0.251 AU (-0.05), a decrease of constriction response in the respiratory sample from 58,5 to 51.9% (-0.074) and the sample with venous occlusion from 65,7 to 55,1% (-0.071). Maximal values of skin blood flow and Ac in response to local heating increased from 17.69 to 21.4 AU (p=0.005), and from 0.318 to 0.491 AU (p=0.069) accordingly.

**Conclusion:** Lipid lowering improves microcirculatory blood flow in patients with CAD, this manifested by: 1) decrease in endothelial, neurogenic and myogenic tone of precapillary arterioles components (if the amplitude of the oscillations of blood flow translate to “tone language”); 2) reduction of microvascular constriction activity of skin; 3) increase vasodilator reserve of skin microcirculation.

#### P1712 | BEDSIDE

No effect modification by cardiovascular risk factors and medication on the efficacy of remote ischemic conditioning in patients with ST-elevation myocardial infarction

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**Purpose:** Remote ischemic conditioning (RIC) induces cardioprotection in patients undergoing primary percutaneous coronary intervention (pPCI) for ST-elevation myocardial infarction (STEMI). Experimental studies of myocardial infarction suggest that the effect of ischemic conditioning may be modulated by cardiovascular risk factors and medication. We evaluated whether cardiovascular risk factors and current medication modified the efficacy of RIC in pPCI-treated patients with STEMI.

**Methods:** We studied 251 patients with STEMI randomized pre-hospitaly to receive pPCI with (n=128) or without (n=125) RIC (intermittent arm ischemia through four cycles of 5-minute inflation and 5-minute deflation of a blood pressure cuff). The primary endpoint was myocardial salvage index (MSI) estimated by single photon emission computed tomography. To assess effect modification, we applied stratified analyses for the difference in myocardial salvage index between the two treatment groups according to cardiovascular risk factors and medication at admission.

**Results:** While the effect tended to be reduced in smokers [difference in MSI in smokers of 0.01 (95% CI: -0.14 to 0.17) versus 0.21 (95% CI: 0.05 to 0.35) in non-smokers], point estimates of improvement in MSI by RIC were consistent in all other subgroups irrespective of the presence of cardiovascular risk factors (Fig. 1) and medication (Fig. 2).

**Conclusion:** RIC is an effective adjunctive treatment to pPCI in STEMI patients regardless of cardiovascular risk factors and current medication.

#### P1713 | BEDSIDE

Remote ischemic preconditioning preserves kidney function in patients with ST-elevation myocardial infarction

T. Yamakawa, Y. Kawai, T. Miyoshi, K. Nakamura, H. Ito. Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

**Background:** Several studies have shown that Remote ischemic preconditioning (RIPC) applied before percutaneous coronary intervention (PCI) in patients evolving ST-elevation myocardial infarction (STEMI) increased myocardial...
salvage. In addition, a recent study showed that RIPC before the use of con-
trast medium prevented contrast-induced acute kidney injury (CI-AKI) in high-risk patients. However, the role of RIPC in reducing CI-AKI in STEMI patients under-
going emergent PCI is not clear. In this study, we evaluated the impact of RIPC on CI-AKI in patients with STEMI who received emergent primary PCI, and hy-
pothesized that RIPC applied before PCI would preserve the kidney function in patients with STEMI.

Methods: This prospective, single-blind, multicenter, randomized, sham-
controlled, parallel-group study was conducted from 2012 to 2013. Consecutive patients with an isolated STEMI were randomly assigned at a 1:1 ratio to re-
ceive percutaneous coronary intervention either with or without RIPC (intermit-
tent arm ischemia through three cycles of 5-minutes inflation and 5-minutes de-
flation of a blood-pressure cuff). The primary endpoint was the incidence of CI-
AKI within 24 hours. SMD was calculated to estimate the increase in serum creatinine (+0.25 to +0.25 mg/dl) over the baseline value in the 48 hours after contrast medium administration. Secondary endpoints were the incidence of major adverse cardiac and cerebral events (MACCE) and the relative change in serum creatinine from baseline to 1 year after PCI.

Results: A total of 125 STEMI patients were enrolled during transfer to primary PCI (63 patients received RIPC before primary PCI and 62 patients received PCI alone). Thirty-one patients did not fulfill the entry criteria and were excluded. A total of 47 RIPC patients and 47 control patients met all study criteria. The incidence of CI-AKI was 10% (n=5) in the RIPC group and 36% (n=17) in the control group (p=0.003). The odds ratio of CI-AKI in patients who received RIPC was 0.18 (95% confidence interval: 0.05–0.64; p=0.008). Seventy-six of the 125 patients with STEMI were available for 1-year follow-up. The incidence of MACCE in 1 year was 18% and 23% (p=0.08) in the RIPC group, and 17% (n=3) in RIPC group versus 23% (n=9) in control group, p=0.06). The relative change in serum creatin-
ine level from baseline at 1 year after PCI was lower in the RIPC group (4.19% increase in RIPC group versus 23.36% increase in the control group, p=0.01).

Conclusions: In patients with STEMI, RIPC before PCI reduced the incidence of CI-AKI and was shown to preserve kidney function in 1-year follow-up.

P1714 | BEDSIDE
Ischemic preconditioning significantly reduces infarct size:
systematic review and meta-analysis of randomized controlled trials
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Cardiac ischemic preconditioning (IPost), defined as rapid intermittent interruptions of blood flow in the early phase of myocardial reperefusion is feasible in pa-
ients with STEMI treated by primary percutaneous coronary intervention (PPCI). IPost significantly reduced infarct size in experimental models and produced con-
trolled reperfusion results in clinical trials. The aim of this systematic review and meta-
analysis was to provide an updated synthesis of the efficacy of IPost on accurate surrogate markers of infarct size.

Randomized controlled trials that evaluated the efficacy of IPost in STEMI patients under reperfusion therapy were identified as an increase in serum creatinine markers of infarct size were considered. Main outcome was the area under the curve (AUC) of serum CK release (CK-AUC). Secondary outcomes were other surrogate biologic markers of infarct size, complete ST-segment resolution (cSTR), direct measure of infarct size by single-photon emission computed tomography (SPECT) or estimate of the infarct size by cardiac magnetic resonance (CMR). Summary measures were reported as standard mean difference (SMD) for continuous variables or risk ratio (RR) for binary variables.

Ten studies were selected including 613 STEMI patients undergoing PPCI with or without IPost. Compared to control, we observed a significant reduction of CK-
AUC (SMD -2.84 95%CI -5.43 to -0.25 IU/L, p=0.03) and cSTR (RR 1.38 95% CI 0.95–1.98, p=0.16). Our meta-analysis suggested that IPost did not significantly
reduce infarct size as estimated by CMR (-0.36 95%CI -0.88 to 0.15 p=0.18).

This meta-analysis dealing with accurate surrogates of infarct size such as CK-
AUC and CMR-IS suggest that IPost reduces infarct size. Whether this trans-
lates into cardiac function and patient’s prognosis improvement still needs to be demonstrated. Larger prospective sufficiently powered randomized controlled trials with clinical endpoints and a standardized protocol to evaluate the efficacy of IPost in STEMI patients are urgently needed.

P1715 | BEDSIDE
Prolonged effect of remote ischemic preconditioning on endothelial function in healthy volunteers and in patients with STEMI
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Aim: In a previous study, we demonstrated that RIPC before PCI improves en-
dotheial function in patients with acute myocardial infarction, and that this effect persists for a week. The aim of the current study was to assess the effect of RIPC on endothelial function in healthy volunteers compared with patients with STEMI.

Methods: Twenty-six healthy volunteers underwent RIPC - by intermittent arm ischemia-reperfusion through four cycles of 5-min inflations and 5-min deflation of a blood-pressure cuff to 200 mm Hg. We assessed endothelial function using the flow-mediated dilation (FMD) test on baseline, after RIPC, and again on days 2 and 7 after PCI. Patients with STEMI were randomly divided into two groups: with or without RIPC prior to primary PCI.

Results: In the group of healthy volunteers at baseline level FMD results was higher than in the STEMI group (10.6% vs. 5.0%, respectively; p=0.005). RIPC improved endothelial function in both the STEMI-RIPC and the healthy volun-
tee group (16.7% vs. 12.3%, respectively; p=0.05), compared with patients with STEMI without RIPC (16.7% vs. 7.6%, respectively; p=0.0004). FMD test results on day 7 in healthy volunteers were considerably higher than in the groups with myocardial infarction with or without RIPC.

Conclusions: RIPC improves endothelial function in healthy volunteers as well as in patients with STEMI, and this effect also remains constant for at least a week. We surmise that the improvement of endothelial function may be one of the explanations of the effect of RIPC.
P1719 | BEDSIDE

Prognostic value of manual thrombus aspiration in patients undergoing Primary Percutaneous Coronary Intervention


Purpose: Recent studies question the value of manual thrombus aspiration (TA) before PCI in patients with ST-segment elevation infarction (STEMI). The aim of this study was to evaluate the impact of TA in a contemporary cohort of patients admitted to our hospital with STEMI who were undergoing primary percutaneous coronary intervention (PPCI).

Methods: We analyzed the data and clinical outcomes of 1044 consecutive patients undergoing PPCI between January 2009 and December 2013. We classified patients into TA-PPCI (n=666) and non TA-PPCI (n=378). Mean follow-up was 23 months. Primary endpoint was all-cause mortality and secondary endpoint was major adverse cardiovascular events (MACE; death, recurrent MI, target vessel revascularization, heart failure).

Results: The median patient age was 65 years, 76.6% were men, 50.1% had hypertension, and 24% had diabetes. Percutaneous access was via the radial approach in 88% of the patients. The culprit artery was the left anterior descending in 44% of the patients, 17.3% had three-vessel disease. The variables independently associated with TA use are: sex, culprit artery, number of vessel disease and TIMI 0 before PPCI.

At the end of the follow-up, 12.5% of the patients died: 11.1% in TA-PPCI group and 15.1% in non TA-PPCI (p=0.040) (See Image 1). The incidence of major adverse cardiovascular events (MACE) at the end of the follow-up was 23.1%: 21% in TA-PPCI group and 23.7% in non TA-PPCI 0.022 (P=0.0022). However, after Cox regression analysis, we don’t find independent association between TA and mortality or MACE.

Conclusions: The use of TA in a “real-world” cohort of patients with STEMI who were undergoing PPCI was not associated with a reduction in mortality or MACE risk.
Methods: Between 2005 and 2008 a total of 7,146 consecutive patients with acute STEMI undergoing primary PCI were prospectively enrolled into the PCI-Registry of the Euro Heart Survey Programme. For the present analysis patients additionally treated with thrombus aspiration (n=897, 12.6%) were compared to those without thrombus aspiration (n=6249, 87.4%).

Results: Patients additionally treated with thrombectomy more frequently presented with shock or had been resuscitated (table). TIMI 0-1 before PCI was much more often found among those with thrombus aspiration. After adjustment for age, female gender, anterior STEMI, prior resuscitation/shock, 3-vessel disease and TIMI 0-1 before PCI thrombectomy was not linked to improved hospital survival rates (odds ratio 0.76, 95% confidence interval 0.52-1.11).

Conclusions: In this real-world registry the use of thrombectomy was quite low. Haemodynamically instable patients were more likely to be treated with thrombus aspiration. In the logistic regression analysis thrombectomy was not associated with an improved prognosis.

**P172 | BEDSIDE**

**Myocardial wash grade: a novel method to evaluate the quality of reperfusion therapy**

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Background: After an acute myocardial infarction, it is important to evaluate the infarct size because it is related to mortality and morbidity. It has previously been shown that there is a good agreement between the QRS scoring system and myocardial infarct size. However, there are few methods to evaluate the quality of reperfusion therapy just on the catheter laboratory. The aim of this study was to evaluate the correlation between the QRS scoring system and Myocardial wash grade.

Methods: Consecutive 61 ST-segment elevation myocardial infarction patients meeting criteria of culprit lesion was proximal or mid portion of left anterior descending artery (LAD), onset-to-door time within 12 hours, and initial Thrombolysis In Myocardial Infarction (TIMI) grade 0 or 1 flow were enrolled in this study. After primary percutaneous coronary intervention, we injected 15ml saline selectively into LAD using an aspiration catheter and electrocardiogram was recorded. The electrocardiographic changes as "Myocardial wash grade" were defined as following 3 types; "Persistent ST elevation", "Terminal T wave inversion", and "Coronary T wave inversion".

Results: The QRS score was significantly lower in a type of "Coronary T wave inversion" compared to a type of "Persistent ST elevation" (P<.0001). There was a good correlation between QRS scoring system and Myocardial wash grade.

Conclusions: Myocardial wash grade is a simple and useful indicator of acute reperfusion quality just on-site.

**P172 | BENCH**

**MPO-deficiency attenuates dilated cardiomyopathy in mice**

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Background: The neutrophil-derived enzyme myeloperoxidase (MPO) has been shown to exert potent pro-inflammatory and pro-fibrotic effects on the vascular and myocardial level. Using muscle Lim protein (MLP)-deficient mice as a model for dilated cardiomyopathy (DCM), we herein sought to evaluate the role of MPO in this disease.

Methods and results: The deposition of MPO within the myocardium was significantly elevated in MLP-deficient (MLP−/−) mice as compared to wildtype littermates (WT) pointing towards a sustained activation of neutrophils in MLP−/− mice. Echocardiography revealed, that MLP−/− mice exhibited a reduction of the fractional shortening (FS, WT vs. MLP−/−: 24.2±1.5 vs. 11.3±1.1, p<0.001) and ejection fraction (EF, WT vs. MLP−/−: -48.4±2.5 vs. 24.7±2.2, p<0.001) compared to WT, as expected. Remarkably, MPO deficiency led to a significant improvement of left ventricular function in MLPxMpo−/− mice as assessed by echocardiography (MLP−/− vs. MLPxMpo−/−: FS; 11.3±1.0 vs. 14.7±1.0, p<0.05; EF; 24.7±2.2 vs. 31.1±1.5, p<0.05) and significantly improved contractility represented by preload recruitable stroke work (MLP−/− vs. MLPxMpo−/−, 40.9±2.2 vs. 59.8±4.6 mmHg*min, p<0.05) determined by left ventricular pressure-volume loops. Reflecting the occurrence of inflammatory processes in failing myocardium, dihydroethidine staining in ventricular sections showed an enhanced ROS production in MLP−/− – as compared to WT mice (3.58±0.7 vs. 1.44±0.35 AU, p<0.05), which was attenuated in MLPxMpo−/− mice (1.55±0.36 AU, p<0.01). Given the potent nitric oxide (NO) consuming properties of MPO, ex-vivo vasoreactivity studies were performed which revealed, that impaired aortic vasodilation in MLP−/− mice (% of relaxation to 100 nM Ach treatment, WT vs. MLP−/− vs. MLPxMpo−/−, -67.22±1.92 vs. -37.51±3.83 vs. -53.98±3.11, p<0.001). This was accompanied by an increased systemic vascular resistance in MLP−/− mice, which was blunted by MPO-deficiency (WT vs. MLP−/− vs. MLPxMpo−/−, 0.35±0.04 vs. 0.56±0.04 mmHg*min*ml−1, p<0.01; MLPxMpo−/− vs. MLP−/−, p<0.01). Conclusions: The current results reveal an improvement of endothelial and left ventricular function by MPO-deficiency in a mouse model of DCM. These data underline the importance of endothelial NO-bioavailability and vascular function in the pathophysiology of cardiomyopathy and emphasize the role of MPO as a potential therapeutic target in this disease.
P1725 | BENCH
Insufficient ATP supply due to excessive degradation of adenine nucleotides by AMP deaminase underlies residual cross-bridges in diastole, leading to diastolic dysfunction in the type 2 diabetic heart
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Purpose: Heart failure with preserved ejection fraction, mostly based on hypercontracted myocardium with altered diastolic properties, is becoming more frequent in diabetic patients. AMP deaminase is known to convert AMP into IMP, which is then converted to adenosine by adenosine kinases. We examined whether AMP deaminase activity and its impact on myocardial mechanics is altered in T2DM.

Methods: Methods: Pressure-volume relationships (PVRs) were determined by a conductance catheter in a model of T2DM, OLETF, and its non-diabetic control, LETO (29-35 weeks old). Pressure overloading was performed by phenylephrine infusions. Heart function was evaluated by cardiac MRI on either 1 Dept. of Cardiology, 2 Dept. of Diabetes Medicine, Hannover Medical School, Hannover, Germany; 3 Heart and Diabetes Center NRW, Bad Oeynhausen, Germany

Results: Heart overloading (OD) for 6 or 12 hours. Echocardiography and left ventricular pressure-volume relationships were measured. Importantly, the CaSpF of HF-Tx CMs treated with AIP was only 0.32±0.14/10-4 m/s, while in control CMs it was 0.73±0.20/10-4 m/s. CaSpF was reduced by 53±10% in HF-Tx (n=110 vs. 76, p<0.05), which translated into a 27±6% decrease in LVEF (n=110 vs. 76, p<0.05). Length and width of Ca2+ sparks were not significantly altered. In sum, CaMKII inhibition reduced the resulting calculated SR Ca2+ leak.

Conclusion: CaMKII inhibition reduced CaSpF (by 63±10% in HF-Tx) and CaSpF in HF-Tx were treated with AIP, which could be neutralized by overexpression of Ubc9. These observations provide evidence that Ubc9 and SUMOylation of SERCA2a is involved in diabetes-mediated exacerbation of left ventricular dysfunction after MI.

P1727 | BENCH
Diabetes blunted the compensatory enhancement of SUMOylation intensity of SERCA2a after MI

Japan

Purpose: Diabetes is an independent risk factor for heart failure and mortality after myocardial infarction (MI). In the condition of diabetes, the activity and expression of Sarcoplasmic Reticulum Calcium-transporting ATPase (SERCA2a) is decreased, leading to diastolic and systolic dysfunction of myocardium. It was recently reported that SUMOylation could elevate the activity and stability of SERCA2a. We assume that diabetes might affect the intensity of SUMOylation of SERCA2a after MI.

Methods: Diet-induced type 2 diabetic rats and controls were divided into survival ligation induced MI groups or sham groups. Primary cardiomyocytes were cultured in different concentrations of glucose and insulin, and underwent myocardial infarction (MI) for 6 or 12 hours. Echocardiography and left ventricular pressure-volume relationships were measured. Importantly, the CaSpF of HF-Tx CMs treated with AIP was only 0.32±0.14/10-4 m/s, while in control CMs it was 0.73±0.20/10-4 m/s. CaSpF was reduced by 53±10% in HF-Tx (n=110 vs. 76, p<0.05), which translated into a 27±6% decrease in LVEF (n=110 vs. 76, p<0.05). Length and width of Ca2+ sparks were not significantly altered. In sum, CaMKII inhibition reduced the resulting calculated SR Ca2+ leak.

Conclusion: Global transcriptomic analysis suggest an early participation of Wnt Signaling in HF progression. Thereby, the expression of different Wnt-Signaling factors seems to be dependent of the disease stage. The finding that the expression of Str2p and Wisp2 correlates with heart function of TAC-mice points to an important role of Wnt-signaling in HF progression.

Heart failure pathophysiology

P1728 | BENCH
The development of LV function upon LVAD-support in human heart failure is linked to the diastolic SR Ca2+ leak
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Purpose: In patients with heart failure (HF) the implantation of a left-ventricular assist device (LVAD) is used to reduce cardiac load and ensure sufficient cardiac output. Whereas most patients can subsequently be weaned from LVAD-support, other patients still need heart transplantation. To elucidate underlying mechanisms we assessed the diastolic SR Ca2+ leak at the time of LVAD implantation (HF-Im), successful LVAD explantation (HF-Ex) and heart transplantation (HF-Tx). Second, we evaluated the effects of CaMKII inhibition on the SR Ca2+ leak in the respective groups.

We obtained left ventricular (LV) myocardial tissue and freshly isolated human cardiomyocytes (CMs) at 1 Hz. To 10 beats to ensure SR Ca2+ loading and scanned for diastolic Ca2+ sparks (confocal microscopy, Fluor-AM). In HF-Im we detected a high diastolic spark frequency (CaSPF) of 0.82±0.13±10-4 m/s which could be reduced to 0.57±0.12±10-4 m/s by CaMKII inhibition with AIP (1 μM). The amplitude of Ca2+ sparks was decreased by 5±1% (n=204 vs. 94, p<0.05). Width and length of Ca2+ sparks were not significantly altered. In sum, CaMKII inhibition reduced the resulting calculated SR Ca2+ leak (CaSPF × duration × width x amplitude) by 60±10% in HF-Im (n=110 vs. 76, P<0.05).

In HF-Tx, we detected an even higher CaSPF of 1.18±0.13±10-4 m/s (P<0.05) and a tendency towards a higher SR Ca2+ leak compared to HF-Im (increase by 53±27%, n=151 vs. 110, P<0.05), which fits to the further decreased LV-function. CaMKII inhibition reduced CaSPF by 63±12% and the calculated SR Ca2+ leak was also significantly reduced. In HF-Tx, CaMKII inhibition with AIP (1 μM) reduced CaSPF by 53±10% and hence lower than in HF-Im (n=33 vs. 150, P<0.05), which translated into a tendency towards a decreased calculated SR Ca2+ leak (n=33 vs. 150, P<0.05). Importantly, the CaSPF of HF-Tx CMs treated with AIP was only 0.32±0.14±10-4 m/s.
4m/s and did not significantly alter from untreated HF-Ex CMs (n=25 vs 33). The SR Ca2+-leak of HF-Tx CMs treated with AIP was even lower than in untreated HF-Ex CMs (P<0.05) due to a smaller spark size.

The present data show that the diastolic SR Ca2+-leak correlates with the development of LV-function after LVAD-implantation and thus may represent an important pathomechanism. The fact that AIP reduces the diastolic SR Ca2+-leak in heart from patients undergoing heart transplantation despite LVAD support to levels lower than in patients who could successfully be weaned from LVAD support suggests that CaMKII inhibition may be a promising therapeutic option to increase the likelihood of a favourable clinical course after LVAD-implantation.

P1729 | BENCH CaMKII equally triggers SR Ca2+-leak in human ischemic and non-ischemic heart failure
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The sarcoplasmic reticulum (SR) Ca2+-leak was shown to be an important pathomechanism in the development of heart failure (HF). It has been attributed to an increased activity of Ca/calmodulin kinase II (CaMKII) leading to a hyperphosphorylation of ryanodine receptor 2 (RYR2). Interestingly, it has recently been suggested in a mouse model that the CaMKII-dependent SR Ca2+-leak is not restricted to non-ischemic HF (DCM) but not in ischemic HF (ICM) which would restrict the treatment with CaMKII inhibitors that are under development to the minority of patients with HF.

We therefore conducted Western blots experiments from 13 ICM- and 21 DCM-patients. In contrast to the non-diabetic mice, we hypothesized that CaMKII may (1) directly influence cardiomyocyte Ca2+-handling and (2) specifically be associated with mortality in patients with acute heart failure (HF).

Methods and results: We measured circulating CAa levels in patients with acute dyspnea due to HF (n=143) and chronic obstructive pulmonary disease (COPD, n=83) and explored the effect of the CaGa fragment catestatin (Cts, CaGα325-372) on cardiomyocyte Ca2+-handling. HF and COPD patients were matched on NYHA functional class (p=0.13) and mortality rates (median 813 days follow-up: 68 HF deaths [46%] vs. 35 COPD deaths [42%], p=0.56), but CaGa levels were only associated with HF mortality (Fig). The association between CaGα levels and HF mortality was also found after adjusting for other risk factors in multivariate Cox regression model: HR logCaGα 1.43 (95% CI 1.11-1.83), p<0.005. By experimental methods, Cts reduced Ca2+-sparks in all dimensions and Ca2+-spark and wave frequency. Cts also increased the magnitude of cardiomyocyte Ca2+-transients and induced larger and faster contractions of cardiomyocytes. Previouly studies have found Cts to be internalized into cells by endocytosis and we observed a direct binding of Cts to the catalytic region of the Ca2+-calmodulin (CaM)-dependent protein kinase II d (CaMMKII), which is a nodal kinase regulating cardiomyocyte Ca2+-handling. Cts also attenuated CaMMKII autophosphorylation in cells and perfused hearts and reduced CaMMKII activity in vitro.

Conclusions: CaGα is a potent risk marker in patients with acute HF and directly associated with cardiomyocyte Ca2+-handling.

P1730 | BENCH Cardiac-specific microRNAs as early modulators in diabetic cardiomyopathy
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Purpose: Diabetic cardiomyopathy (DCM) accounts for more than 50% of deaths in diabetic patients. Despite all the efforts made to address this global burden, the high incidence of DCM remains a challenge to the clinicians. Importantly, heart diseases develop at a much earlier stage, but is often unrecognized in the subclinical stage due to the absence of pathognomonic signs, thereby restricting its early detection and active therapeutic management. Identifying the early modulators in DCM will not only help in early detection of the disease, but also allow sufficient time for optimization of the treatment. Recently microRNAs (miRs) and their pathophysiology of several diseases including cardiovascular diseases. However, the pathophysiological role of miRs in the development of DCM is unknown. Therefore, the aim of this study was to (i) investigate the modulation of cardiac-specific miRs with the evolution of DCM and (ii) demonstrate the association between the changes in miRs and development of cardiac dysfunction.

Methods: BKS.Cg+/-m+/LeprobJr mice were used as a model of type-2 diabetes which develop cardiac dysfunction as a result of high glucose and best represents type-2 diabetes. At the age of 8 week of age which continued with the progression of the disease. Importantly, echocardiographic assessment of cardiac function at this time point failed to reveal any changes, with first clinically detectable diastolic dysfunction (alteration in E/A ratio) observed only after 20 weeks of age (P<0.05 vs. non-diabetic).

Conclusions: Our initial findings provide a strong evidence for modulation of cardiac specific miRs at an early stage of diabetes and opens up an intriguing possibility to develop miR-based therapies for timely management of the disease. A larger study is underway to confirm these findings.

P1733 | BENCH Chromogranin A is a potent risk marker in acute heart failure and directly associated with cardiomyocyte Ca2+-handling
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Background: Chromogranin A is considered as an unspecific prognostic biomarker, but given the established role of granin proteins on Ca2+-handling in cardiomyocytes, we hypothesized that CaGα may (1) directly influence cardiomyocyte Ca2+-handling and (2) specifically be associated with mortality in patients with acute heart failure (HF).

Methods and results: We measured circulating CaGα levels in patients with acute dyspnea due to HF (n=143) and chronic obstructive pulmonary disease (COPD, n=83) and explored the effect of the CaGα fragment catestatin (Cts, CaGα325-372) on cardiomyocyte Ca2+-handling. HF and COPD patients were matched on NYHA functional class (p=0.13) and mortality rates (median 813 days follow-up: 68 HF deaths [46%] vs. 35 COPD deaths [42%], p=0.56), but CaGα levels were only associated with HF mortality (Fig). The association between CaGα levels and HF mortality was also found after adjusting for other risk factors in multivariate Cox regression model: HR logCaGα 1.43 (95% CI 1.11-1.83), p<0.005. By experimental methods, Cts reduced Ca2+-sparks in all dimensions and Ca2+-spark and wave frequency. Cts also increased the magnitude of cardiomyocyte Ca2+-transients and induced larger and faster contractions of cardiomyocytes. Previouly studies have found Cts to be internalized into cells by endocytosis and we observed a direct binding of Cts to the catalytic region of the Ca2+-calmodulin (CaM)-dependent protein kinase II d (CaMMKII), which is a nodal kinase regulating cardiomyocyte Ca2+-handling. Cts also attenuated CaMMKII autophosphorylation in cells and perfused hearts and reduced CaMMKII activity in vitro.

Conclusions: CaGα is a potent risk marker in patients with acute HF and directly associated with cardiomyocyte Ca2+-handling.
including fibrosis and improved the survival in dnNRSF-Tg. Arrhythmogenicity was substantially reduced in dnNRSF-Tg with DRI. Genetic deletion of angiotensin type 1a receptor (AT1aR) in dnNRSF-Tg prevented cardiac remodeling and SCD. In optical mapping analyses, spontaneous ventricular tachycardia (VT) and fibrillation (VF), which are initiated by a breakthrough-type focal activation and maintained by functional reentry, were observed in hearts of dnNRSF-Tg (Figure). Under constant pacing, dnNRSF-Tg hearts exhibited remarkably slowed conduc-
tion velocity contributing to generating arrhythmogenic substrates. DRI restored the conduction velocity and reduced the incidence of sustained VT. Furthermore, dnNRSF-Tg ventricles showed markedly reduced protein expression of connexin 43, which was restored with DRI.

Conclusions: Renin inhibition or genetic deletion of AT1aR prevented patholog-
cal cardiac remodeling that leads to the generation of substrates to VT/VF and reduced the occurrence of SCD in dnNRSF-Tg. Our findings demonstrate the sig-
nificant contribution of RAS activation to promoting arrhythmogenic remodeling.

P1734 | BENCH RNA-seq analysis reveals new significant alterations in transcriptional regulators of patients with ischemic cardiomyopathy

Methods: RNA-sequencing analysis reveals new significant alterations in P1734 | BENCH transcriptional regulators of patients with ischemic cardiomyopathy (ICM). The aim of this study was to identify new transcription regulators (TFs) to provide insights into the molecular mechanisms involved in the responses to ischemia, using RNA-sequencing analysis (RNA-Seq).

Methods: We analyzed by RNA-seq and qRT-PCR left ventricular tissue from 24 index patients and 17 from patients with ICM and 7 control subjects. Functional analysis of differentially expressed genes was performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID, version 6.7). We se-
lected the gene ontology (GO) terms that had a p-value of ≤0.05.

Results: Significance analysis of the RNA-Seq results revealed a total of 1249 genes that were differentially expressed in ICM patients; 602 genes were up-
regulated (≥1.5 fold, p<0.05) and 647 genes were down-regulated (≤1.5 fold, p<0.05).

Conclusions: The alterations found in SP100, BCL3, CITED2, and CEBPD, con-
firmations occurring in ICM. Our results provide a new regulatory network in ICM.
Changes in CITED2 mRNA levels were related with LV function (p<0.01).

P1735 | BEDSIDE Endomyocardial infiltration of macrophages, but not T lymphocytes, is associated with poor long-term prognosis in patients with dilated cardiomyopathy without severe cardiac fibrosis

Methods: Of the patients admitted to our hospital with heart failure in 2005, sub-
jects who were finally diagnosed as having DCM by excluding hypertrophic car-
diomyopathy, ischemic cardiomyopathy, valvular heart disease, myocarditis, and secondary cardiomyopathy, were included in the study. Thirty-eight patients with LVEF <40% were analyzed. Paraaffin-embedded right ventricular endomyocardial biopsy specimens were retrieved with ICD. Trichrome and specific antibody to CD68 (macrophages) and CD3 (T lymphocytes). The collagen volume frac-
tion (CVF) was calculated as the area occupied by collagen divided by the total area, and the numbers of macrophages and T lymphocytes infiltrated to the my-
cocardium were counted in each sample. Also, patients' clinical data were obtained by reviewing the medical records. Those patients were observed for up to 8 years. Adverse events were defined as death or readmission for heart failure.

Results: The mean age was 50.1±15 years and 79% were men. Left ventricular EF was 28±10% with 42% of patients having NYHA class II or IV. Mean CVF in endomyocardial sections was 22±11%. We divided patients into two groups; 1) severe fibrosis: CVF ≥20%, n=19, and 2) less severe fibrosis: CVF <20%, n=19. During the follow-up period, 8 patients with severe fibrosis and 6 patients with less severe fibrosis had experienced adverse events (42 vs. 32%, p=NS). In less severe fibrosis group, patients with adverse events showed greater number of CD68-positive macrophages infiltration than those without (60.1±27 vs. 33±1 mm², p=0.011) but comparable number of CD3-positive T lymphocytes (25±27 vs. 22±23/mm², p=NS). On the other hand, the difference of infiltrated macrophages (45±24 vs. 4.1±25/mm², p=NS) and T lymphocytes (33±34 vs. 28±30/mm², p=NS) was not observed in severe fibrosis group.

Conclusions: In patients with DCM without severe cardiac fibrosis, infiltrated macrophages, but not T lymphocytes, were associated with long-term adverse outcome, indicating a role of macrophages in LV remodeling in patients with DCM.

P1736 | BENCH Changes in microRNAs could explain the dysfunction of the cardiac conduction system (CCS) in heart failure

Methods: Adverse events were defined as death or readmission for heart failure.

Results: Increased HF and 34% in control

Conclusions: The alterations found in SP100, BCL3, CITED2, and CEBPD, con-
firmations occurring in ICM. Our results provide a new regulatory network in ICM.
Changes in CITED2 mRNA levels were related with LV function (p<0.01).

P1735 | BEDSIDE Endomyocardial infiltration of macrophages, but not T lymphocytes, is associated with poor long-term prognosis in patients with dilated cardiomyopathy without severe cardiac fibrosis

Methods: Of the patients admitted to our hospital with heart failure in 2005, sub-
jects who were finally diagnosed as having DCM by excluding hypertrophic car-
diomyopathy, ischemic cardiomyopathy, valvular heart disease, myocarditis, and secondary cardiomyopathy, were included in the study. Thirty-eight patients with LVEF <40% were analyzed. Paraaffin-embedded right ventricular endomyocardial biopsy specimens were retrieved with ICD. Trichrome and specific antibody to CD68 (macrophages) and CD3 (T lymphocytes). The collagen volume frac-
tion (CVF) was calculated as the area occupied by collagen divided by the total area, and the numbers of macrophages and T lymphocytes infiltrated to the my-
cocardium were counted in each sample. Also, patients' clinical data were obtained by reviewing the medical records. Those patients were observed for up to 8 years. Adverse events were defined as death or readmission for heart failure.

Results: The mean age was 50.1±15 years and 79% were men. Left ventricular EF was 28±10% with 42% of patients having NYHA class II or IV. Mean CVF in endomyocardial sections was 22±11%. We divided patients into two groups; 1) severe fibrosis: CVF ≥20%, n=19, and 2) less severe fibrosis: CVF <20%, n=19. During the follow-up period, 8 patients with severe fibrosis and 6 patients with less severe fibrosis had experienced adverse events (42 vs. 32%, p=NS). In less severe fibrosis group, patients with adverse events showed greater number of CD68-positive macrophages infiltration than those without (60.1±27 vs. 33±1 mm², p=0.011) but comparable number of CD3-positive T lymphocytes (25±27 vs. 22±23/mm², p=NS). On the other hand, the difference of infiltrated macrophages (45±24 vs. 4.1±25/mm², p=NS) and T lymphocytes (33±34 vs. 28±30/mm², p=NS) was not observed in severe fibrosis group.

Conclusions: In patients with DCM without severe cardiac fibrosis, infiltrated macrophages, but not T lymphocytes, were associated with long-term adverse outcome, indicating a role of macrophages in LV remodeling in patients with DCM.
P1737 | BENCH
Disruption of oxidative PKA activation contributes to ventricular remodeling upon increased afterload

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Recently, a novel CaM-dependent protein kinase (PKA) activating pathway by oxidative stress was identified. We hypothesized that redox-activated PKA is involved in cardiac remodeling upon pathological afterload. Homozygous knock-in mice with Rlu cysteine 17 to serine mutation (KI), which are devoid of oxidation-dependent activation, were subjected to transverse aortic constriction (TAC) and compared with wild-type (WT). At baseline, echocardiographic analysis revealed identical myocardial function and morphology (Fig. 1). Six weeks after TAC, however, KI mice showed significantly more compromised ejection fraction and accelerated left ventricular dilation (Fig. 1). Moreover, Kaplan-Meier analysis showed exaggerated mortality after TAC in KI vs. WT mice (Fig. 1). In vivo analysis of arrhythmia inducibility, catheters were inserted into the right ventricle. Compared to WT, burst stimulation at the apex induced more ventricular arrhythmias in KI mice (Fig. 1). Confocal microscopy of isolated ventricular myocytes showed no difference in Ca spark frequency (not shown). However, L-type Ca currents (ICa) were significantly larger in KI mice (for KI vs. WT, 7.8±0.4 vs. 6.4±0.2 A/F; n=14 vs. 11). Interestingly, Ca2+-transients were significantly lower in KI myocytes (for KI vs. WT, 653.6±109.9 vs. 1158±163 jmol/L, n=21 vs. 12). Ca transient decay (τ) was significantly prolonged in KI vs. WT indicating a reduced SERCA function (at 0.5Hz, 0.55±0.02 s vs. 0.37±0.02 s; n=14 vs 23). KI mice were designed to have a reduced expression of cytosolic Ca2+-ATPase. Hence, we measured Ca2+ transient decay in isolated ventricular myocytes (for KI vs. WT, 0.5±0.02 s vs. 0.37±0.02 s; P<0.001). Correspondingly, the rightward shift of the pressure-volume curve of amplitude: 8.5% vs 12.5%; P<0.05), Cmax-3 (P<0.01), and were smaller in HF compared to sham. In addition, a reduced expression of CD3 (P<0.05), and Mac-3 (P<0.01). When treated with MM284, parallel in the evaluation of Masson’s Trichrome staining also showed a reduction of the cardiac fibrosis (P<0.05), when treated. In addition expression of MMP-9 was significantly reduced. In vitro migration of human monocytes was assessed using a modified Boyden chamber. In the presence of MM284, migration towards extracellular CyPA was almost completely abolished (P<0.01). Finally analysis of biopsy samples of patients with non ischemic cardiomyopathy revealed that severe cardiac fibrosis was associated with the expression of CyPA. Conclusion: Extracellular CyPs, especially CyPA play an important role in inflammatory and profibrotic processes. In the current study we found that the extracellular ligation of CyPs via MM284 is a successful and potent pharmacological approach for the treatment of myocardial inflammation and reduction of cardiac fibrosis.

P1738 | BENCH
Deficiency of MAP-kinase-activated protein kinase 2 (MK2) targeting mitochondrial oxidative stress protects against aging-induced cardiac remodeling and dysfunction

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Background: Cyclicolphins (CyPs) are a group of highly conserved cytosolic enzymes that have a peptidylprolyl isomerase activity. This study analyzed the effect of the Cycolsporin A derivative MM284 in a mouse model of autoimmune myocarditis. Due to the modulation of Cycolsporin A a cyclophilin inhibitor, MM284 strictly blocks extracellular activities of Cyclicolpins such as CyPA. Methods and results: AJ mice were immunized with murine cardiac troponin I (mCTnI) at day 0, 7, and 14. Mice were treated with MM284 or 0.29 A/F, and Mac-3 (P<0.01), and were smaller in HF compared to sham. In addition, a reduced expression of CD3 (P<0.05), and Mac-3 (P<0.01). When treated with MM284, parallel in the evaluation of Masson’s Trichrome staining also showed a reduction of the cardiac fibrosis (P<0.05), when treated. In addition expression of MMP-9 was significantly reduced. In vitro migration of human monocytes was assessed using a modified Boyden chamber. In the presence of MM284, migration towards extracellular CyPA was almost completely abolished (P<0.01). Finally analysis of biopsy samples of patients with non ischemic cardiomyopathy revealed that severe cardiac fibrosis was associated with the expression of CyPA. Conclusion: Extracellular CyPs, especially CyPA play an important role in inflammatory and profibrotic processes. In the current study we found that the extracellular ligation of CyPs via MM284 is a successful and potent pharmacological approach for the treatment of myocardial inflammation and reduction of cardiac fibrosis.

P1739 | BENCH
The novel extracellular CyPA-inhibitor MM284 reduces myocardial inflammation and remodelling in a mouse model of Troponin-I-induced myocarditis

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Background: Heart failure (HF) is a major risk factor of atrial fibrillation (AF) by favoring structural remodeling of the myocardium and changes in ion currents which together compose AF substrate. Here we studied the role played by tissue factors and ion current modifications in the alterations of atrial electrical properties during HF.

Methods: HF was induced in rats by coronary ligation. Atrial remodeling was studied by echography and ECG. The substrate was evaluated by the duration of episode of AF triggered by burst pacing delivered by a transesophageal probe. To study the electrical activity of myocytes in situ, the propagated action potential (AP) was recorded by using standard microelectrode in trabeculae. Ion currents were recorded in whole cell patch clamp. The various parameters were quantified by their coefficient of variation (Cvar; ratio of standard deviation/mean expressed in %). Computer model to simulate an atrial AF was derived from Courtemanche et al. model.

Results: Two months after surgery all rats were in HF by coronary ligation. Atrial remodeling was studied by echography and ECG. The substrate was evaluated by the duration of episode of AF triggered by burst pacing delivered by a transesophageal probe. To study the electrical activity of myocytes in situ, the propagated action potential (AP) was recorded by using standard microelectrode in trabeculae. Ion currents were recorded in whole cell patch clamp. The various parameters were quantified by their coefficient of variation (Cvar; ratio of standard deviation/mean expressed in %). Computer model to simulate an atrial AF was derived from Courtemanche et al. model.

Figure 1

In conclusion: Mice lacking oxidative activation of PKA show a profound dysregulation of excitation-contraction coupling and an increased propensity for arrhythmias. Moreover, they display an enhanced ventricular remodeling upon TAC. This may be of relevance for the treatment of arrhythmias and HF.

P1740 | BENCH
Alteration of atrial myocyte environment is a minor determinant of the action potential remodeling of dilated atria during heart failure in rat

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Methods: HF was induced in rats by coronary ligation. Atrial remodeling was studied by echography and ECG. The substrate was evaluated by the duration of episode of AF triggered by burst pacing delivered by a transesophageal probe. To study the electrical activity of myocytes in situ, the propagated action potential (AP) was recorded by using standard microelectrode in trabeculae. Ion currents were recorded in whole cell patch clamp. The various parameters were quantified by their coefficient of variation (Cvar; ratio of standard deviation/mean expressed in %). Computer model to simulate an atrial AF was derived from Courtemanche et al. model.

Results: Two months after surgery all rats were in HF by coronary ligation. Atrial remodeling was studied by echography and ECG. The substrate was evaluated by the duration of episode of AF triggered by burst pacing delivered by a transesophageal probe. To study the electrical activity of myocytes in situ, the propagated action potential (AP) was recorded by using standard microelectrode in trabeculae. Ion currents were recorded in whole cell patch clamp. The various parameters were quantified by their coefficient of variation (Cvar; ratio of standard deviation/mean expressed in %). Computer model to simulate an atrial AF was derived from Courtemanche et al. model.

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been previously shown to be drastically reduced in this model. HF atria showed a higher expression of fibronectin (fibrosis) and vimentin (fibroblast). Computer simulation indicated that AF shortening was caused by the unbalance between ICA and IK during the plateau phase whereas the depressed and dispersed excitability is predominantly due to electronic interactions between myocyte and coupled cardiomyocytes, cell hypertrophy and gap junction reduction.

Conclusion: Alterations in the normal environment of atrial myocyte is a major determinant of the atrial electrical remodelling and AF substrate during HF.

P1741 | BENCH
Neuregulin-1 has opposite effects on LV compliance in eccentric and concentric remodelling
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Introduction: There is emerging evidence that left ventricular (LV) diastolic stiffness may be caused by factor-induced cardiac endothelial dysfunction. To date, most studies have focused on impaired nitric oxide (NO) and cyclic GMP signalling, and on the effects by pharmacologic rescue of these pathways. In this study, we examined the effect of neuregulin-1 (NRG-1), an endothelial secreted ligand of ErbB4 receptors, on LV diastolic compliance in mice. Effects of ErbB4 activation on LV compliance were studied in (a) normal hearts, (b) stiff hearts (with concentric LV hypertrophy) and (c) hypercontractile hearts (with eccentric LV remodelling).

Methods: RhNRG-1 or vehicle was administrated (20 μg/kg/day, i.p., 5 days/week) in 3 groups. (a) Healthy C57Bl/6 mice (n=56), (b) C57Bl/6 mice with eccentric LV remodelling [resulting in 50% LV diameter reduction (LVEDD)] after 4 weeks), (c) C57Bl/6 mice with concentric LV remodelling (n=59), induced by angiotensin II (osmotic mini-pump, 1000 ng/kg/day, for 4 weeks) and (c) C57Bl/6 mice with eccentric LV remodelling (n=66) (streptozotocin-induced type 1 diabetes, 14 weeks follow-up). In vivo, LV diameters and LV diastolic compliance (slope EDPVR) were quantified by echocardiography and LV pressure-volume recordings. Ex vivo, LV collagen volume fraction (CVFR) and cardiomyocyte diameters (MyoDia) were quantified by immuno-histochemistry. Stiffness of isolated skinned cardiomyocytes was quantified. Activation of cardiac ErbB4 receptors by rhNRG-1 was verified in each model.

Results: In the normal heart, rhNRG-1 failed to change LV diameters, LV diastolic and cardiomyocyte stiffness, both in acute (30 min) and in chronic (14 week) experiments. In Ang II-treated mice, rhNRG-1 prevented the development of concentric LV hypertrophy, cardiomyocyte hypertrophy (MyoDia 13.17 ± 17.25 μm, p < 0.01), cardiomyocyte stiffening, LV fibrosis (CVFR 0.056 vs 0.152 FR%, p < 0.05) and LV stiffening (slope EDPVR 0, 396 vs 0, 586 mmHg/L, p < 0.05). In type 1 diabetic mice, rhNRG-1 prevented LV dilation (LV end diastolic diameter 13.57 ± 0.01 μm, p < 0.001), LV contractile dysfunction (slope ESPVR 23.68 vs 4.31 mmHg/L, p < 0.001) and LV hypercompliance (slope EDPVR 0.473 vs 0.176 mmHg/L, p < 0.05), but it had no effect on LV fibrosis.

Conclusion: rhNRG-1 does not change LV structure or LV compliance of the healthy heart. By contrast, rhNRG-1 prevented LV stiffening during concentric remodelling and prevents LV de-stiffening during eccentric remodelling. These circumspection-dependent protective effects by rhNRG-1 on LV compliance attribute unique therapeutic opportunities of ErbB4 stimulation during LV remodelling.

P1742 | BEDSIDE
QRS fragmentation as predictor for reverse remodelling in cardiac resynchronization therapy patients

Background: About 1/3 of patients do not respond clinically to cardiac resynchronization therapy (CRT), and >40% do not show LV reverse remodelling response. QRS fragmentation (QRSf) on ECG has been related with disturbances in LV diastolic and systolic function due to myocardial fibrosis. Role of QRSf as predictor of CRT response is controversial and has not been widely studied.

Methods: We reviewed clinical records of patients who underwent CRT implantation in our Institution. QRSf was defined as the presence of RSR' pattern, notching of the R-wave or notchting of the down- or upstroke of the S-wave in two contiguous leads.

Results: 40 patients (71 ± 10 years, male 80%). At inclusion, QRSf was present in 25 patients (82.5%). There were no differences in baseline characteristics. Table. After a mean follow-up of 24 ±13 months patients with QRSf showed a significant reduction in left ventricular end-diastolic diameter (LVEDD) after biventricular pacing (60.7 ± 17 mm vs 51.9 ± 8 mm; p < 0.05) vs patients without QRSf (62.8 ± 18 mm vs 58.7 ± 10 mm; p < 0.05). No difference in improvement of EF or clinical events. Univariate analysis showed that QRSf was independent predictor of LV EDD reduction (OR 0.15 [0.02-0.99], p < 0.05).

Conclusions: The presence of QRSf was a predictor of reverse remodelling expressed as LVEDD reduction. Biventricular pacing can improve hemodynamics in patients with severe intraventricular conduction disturbances expressed as QRSf.

P1743 | BEDSIDE
Diffuse myocardial fibrosis assessed by cardiac magnetic resonance contrast-enhanced T1 mapping in heart failure with preserved ejection fraction
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Purpose: To determine the pathophysiology of heart failure with preserved ejection fraction (HFpEF) remains to be clarified. We sought to assess myocardial fibrosis, measured as extracellular volume (ECV) of the myocardium by using cardiac magnetic resonance (CMR) T1 mapping, in acutely decompensated heart failure (ADHF) with preserved ejection fraction. Methods: Twenty-nine ADHF subjects (20men, 61 ±20years) and 15 control subjects with normal CMR findings were prospectively enrolled. Triple-slice T1 mapping was performed by using a modified Look-Locker inversion recovery (MOLLI) sequence. ECV was quantified using hematocrit-adjusted myocardial and blood T1 values measured before and after administration of gadolinium contrast medium.

Results: Thirteen (45%) patients had HFpEF. Patients with HFpEF had significantly greater mean ECV, pre-contrast T1 than control group (31.6 ±7.4 vs 26.9 ±3.0%, 1372 ±86 vs 1305 ±34ms, respectively, p <0.05). However, there were no significant differences in mean ECV and pre-contrast T1 value between HFpEF and HF with reduced ejection fraction (HFrEF-34.8 ±7.1%, 1374 ±70ms, respectively). Univariate analysis demonstrated that ECV was associated with the presence of late gadolinium enhancement, the ratio of early transmirtal velocity to Doppler mitral annular early diastolic velocity (E/Ea), and B-type natriuretic peptide level (r=0.39, 0.53, 0.78, respectively, all p<0.05). High E/Ea was a significant predictor of ECV expansion (r=0.39, 0.53, p <0.05).

Figure 1. Representative causes.

Conclusion: The results with CMR quantification of ECV demonstrated that diffuse myocardial fibrosis was independently associated with LV filling pressures in patients with HFpEF.

P1744 | BEDSIDE
Plasma biomarkers as surrogates of myocardial fibrosis
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Purpose: Plasma biomarkers have been proposed to reflect fibrosis of several human tissues, but their specific role in detection of myocardial fibrosis has not been well established. We studied the association between galectin-3, PIIINP, PINP and myocardial fibrosis measured by late gadolinium enhanced cardiac magnetic resonance imaging (MRI) and their relation to left ventricular (LV) diastolic filling measured by tissue Doppler echocardiography in patients with stable coronary artery disease (CAD).

Methods and results: We determined the galectin-3, PIIINP, and PINP plasma levels and performed cardiac MRI and tissue Doppler echocardiography in 64 pa-

Table 1. Patients characteristics according to QRS fragmentation

<table>
<thead>
<tr>
<th>No QRSf (15)</th>
<th>QRSf (25)</th>
<th>p</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>69±10</td>
<td>72±10</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>13 (86%)</td>
<td>19 (76%)</td>
</tr>
<tr>
<td>Ischemic Cardiomyopathy</td>
<td>9 (60%)</td>
<td>13 (52%)</td>
</tr>
<tr>
<td>NYHA (III-IV)</td>
<td>10 (71%)</td>
<td>14 (58%)</td>
</tr>
<tr>
<td>Serum Rhythm</td>
<td>9 (60%)</td>
<td>12 (48%)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>23 ±7</td>
<td>21 ±7</td>
</tr>
<tr>
<td>Clinical follow-up</td>
<td>36±11</td>
<td>33±13</td>
</tr>
<tr>
<td>HF admissions</td>
<td>5 (33%)</td>
<td>5 (20%)</td>
</tr>
<tr>
<td>NYHA (III-IV)</td>
<td>4 (26%)</td>
<td>2 (8%)</td>
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<tr>
<td>EF</td>
<td>29±12</td>
<td>33±13</td>
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tients with stable CAD without a history of prior myocardial infarction. Extraceellular volume assessed from myocardial late gadolinium enhancement T1 relaxation time was defined as a specific marker of myocardial fibrosis. PNP and PIINP did not have a significant correlation with the T1 relaxation time (NS for both), but there was a significant correlation between T1 relaxation time and gate=10 (r² = 0.33, p = 0.012). The early to late tissue velocity ratio (E/E') was related to both gate=10 (r² = 0.39, p < 0.001) and PIINP (r² = 0.33, p < 0.001). The lowest T1 relaxation time tertile had a significantly higher gate=10 levels (p = 0.009) and higher E/E' values (p = 0.048) compared to the highest T1 relaxation time tertile.

Conclusions: Elevated plasma levels of gate=10 reflect the degree of myocardial fibrosis assessed by MRI and LV diastolic dysfunction, suggesting that this biomarker is a useful surrogate of structural and functional abnormality of the myocardium.

P1747 | BENCH
Remodeling of cardiac sympathetic innervation with thoracic spinal cord stimulation improves left ventricular function in a porcine model of ischemic cardiomyopathy
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Background: Prior studies demonstrate that thoracic spinal cord stimulation (SCS) improves left ventricular (LV) function in heart failure (HF), nevertheless, the mechanism of action remains unknown.

Methods and results: We performed chronic thoracic SCS (50Hz, pulse width 0.2ms) using two octrode leads implanted targeting along the midline and the left side at T1-3 levels in 30 adult pigs with ischemic HF induced by myocardial infarction and rapid ventricular pacing for 4 wks. All animals were treated with daily oral metoprolol succinate (25mg) plus ramipril (2.5mg), and randomized into control group (n=10), intermittent SCS (4 hrs x 3, n=10) or continuous SCS (24 hrs, n=10) for 10 weeks. Detailed immunohistological studies on myocardial sympathetic (tyrosine hydroxylase [TH]) and parasympathetic (acetylcholinase [Ach]) nerve spouting (growth-associated protein43 [GAP-43]) and nerve innervation (protein gene product 9.5 [PGP9.5]) were performed at infarct, peri-infarct and normal regions. Both continuous and intermittent SCS significantly improved LV ejection fraction at 10 wks compared with controls (P < 0.05). There was no significant difference in pattern of the Ach staining over different regions between 3 groups. However, SCS-treated groups showed diffuse sympathetic nerve spouting over the infarct, peri-infarct and normal regions. Both continuous and intermittent SCS significantly improved LV ejection fraction at 10 wks compared with controls (P < 0.05). There was no significant difference in pattern of the Ach staining over different regions between 3 groups. However, SCS-treated groups showed diffuse sympathetic nerve spouting over the infarct, peri-infarct and normal regions. Both continuous and intermittent SCS significantly improved LV ejection fraction at 10 wks compared with controls (P < 0.05). There was no significant difference in pattern of the Ach staining over different regions between 3 groups. However, SCS-treated groups showed diffuse sympathetic nerve spouting over the infarct, peri-infarct and normal regions.

Conclusions: SARCA2a gene transfer, a novel therapeutic approach to treat heart failure, can prevent progressive remodeling in chronic heart failure.

Methods: An extensive anterior myocardial infarction (MI) was induced in Yorkshire pigs. One month after the MI induction, pigs developed chronic heart failure as characterized by impaired LV ejection fraction, dilated LV, and increased end-diastolic pressure. The animals were randomly assigned to receive intracoronary injection of either saline or adeno-associated virus-1 SARCA2a (3.0×1012 v.p.). LV volumes were assessed by 3-dimensional echocardiography by a blinded investigator. LV volumes were indexed to body surface area and changes before and 2 months after the gene transfer were evaluated.

Results: A total of 31 pigs were included in the study (SARCA2a n=16, Saline n=15). LV ejection fraction (EF) improved in SARCA2a gene transfer group with events (HR 1.036; 95% CI 1.005-1.068; P = 0.021), but not in HFpEF group (HR 1.006; 95% CI 0.960-1.053; P = 0.815).

Conclusions: LA size on admission can predict future events in patients with HFpEF but not in HFpEF. Patients with larger LA size in HFpEF need to be paid more attention.
DIADEMS AND HEART FAILURE

P1750 | BEDSIDE
Insulin resistance is associated with impaired cardiac sympathetic innervation in patients with heart failure
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Purpose: Insulin resistance (IR) represents cause and consequence of heart failure (HF) and affects prognosis in HF patients, but pathophysiological mechanisms remain to be understood. In this study, considering that cardiac sympathetic drive and insulin are known to be associated with IR, we aimed to evaluate the presence of IR in patients with heart failure.

Methods: Ninety-five patients (88% males; 64.8 ± 11.1 years) with severe-to-moderate HF (ejection fraction 32.4 ± 9.6%), underwent iodine-123 metaiodobenzylguanidine (123I-MIBG) scintigraphy to assess sympathetic innervation and Homeostasis Model Assessment Insulin Resistance (HOMA-IR) value to determine the presence of IR. From 123I-MIBG imaging early and late heart to mediastinum (H/M) ratios were calculated.

Results: Fifty-eight (61%) patients showed IR and 37 (39%) were non-IR. No significant differences between IR and non-IR patients were found for age, ejection fraction, NYHA class, HF etiology and cardiac sympathetic innervation in non diabetic HF patients.

Conclusion: Cardiac sympathetic innervation is more impaired in patients with IR and HF compared to matched non-IR patients. These findings contribute to explain the unfavorable prognostic impact of IR in patients with HF.

P1754 | BEDSIDE
Influence of pancreatic β-cell function on left ventricular remodeling in type 2 diabetes mellitus patients
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Purpose: To investigate the impact of pancreatic β-cell function on left ventricular remodeling in type 2 diabetes mellitus (T2DM) patients.

Methods: Ninety-five patients (88% males; 64.8±11.1 years) with severe-to-moderate HF (ejection fraction 32.4±9.6%), underwent iodine-123 metaiodobenzylguanidine (123I-MIBG) scintigraphy to assess sympathetic innervation and Homeostasis Model Assessment Insulin Resistance (HOMA-IR) value to determine the presence of IR. From 123I-MIBG imaging early and late heart to mediastinum (H/M) ratios were calculated.

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Conclusion: Cardiac sympathetic innervation is more impaired in patients with IR and HF compared to matched non-IR patients. These findings contribute to explain the unfavorable prognostic impact of IR in patients with HF.

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P1752 | BEDSIDE
Natriuretic peptides or glycosolated haemoglobin as markers of micro- and macro-vascular complications amongst older patients with type 2 diabetes mellitus. a report from sica-diabetes study
1. Department of Medicine, St George’s University Hospital, London, United Kingdom; 2. Department of Geriatric Medicine, St George’s University Hospital, London, United Kingdom; 3. Department of Health Sciences, University of York, York, UK

Purpose: To investigate the use of natriuretic peptides or glycosolated haemoglobin as markers of micro- and macro-vascular complications amongst older patients with type 2 diabetes mellitus.

Methods: Ninety-five patients (88% males; 64.8±11.1 years) with severe-to-moderate HF (ejection fraction 32.4±9.6%), underwent iodine-123 metaiodobenzylguanidine (123I-MIBG) scintigraphy to assess sympathetic innervation and Homeostasis Model Assessment Insulin Resistance (HOMA-IR) value to determine the presence of IR. From 123I-MIBG imaging early and late heart to mediastinum (H/M) ratios were calculated.

Results: Fifty-eight (61%) patients showed IR and 37 (39%) were non-IR. No significant differences between IR and non-IR patients were found for age, ejection fraction, NYHA class, HF etiology and cardiac sympathetic innervation in non diabetic HF patients.

Conclusion: Cardiac sympathetic innervation is more impaired in patients with IR and HF compared to matched non-IR patients. These findings contribute to explain the unfavorable prognostic impact of IR in patients with HF.

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P1753 | BEDSIDE
Favorable impact of pancreas transplant alone on left ventricular diastolic function and left ventricle mass in type 1 diabetes patients
L. Rondinini1, P. Giordano2, C. Alderighi1, E. Favilli1, N. Scelza1, L. Stazzoni1, M. Occhipinti2, U. Boggi2, P. Marchetti2, R. Mariotti1, R. Mariotti1
1. Department of Advanced Biomedical Sciences, Section of Cardiology, Federico II University of Naples, Naples, Italy; 2. Division of Cardiology, Salvatore Mangano Foundation, Institute of Cardiology (BN), Naples, Italy

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P1751 | BENCH
Sitagliptin improves diastolic function an increases glucose uptake in the diabetic myocardium
E. Ramirez1, B. Picatoste1, M.A. Murcillo1, A. Caro1, J. Egedis1, J. Tunon Fernandez2, O. Lorenzo1
1. Foundation Jimenez Diaz, Madrid, Spain; 2. CICIMAT, Madrid, Spain; 3. School of Veterinary Sciences, Complutense University, Madrid, Spain

Purpose: Glucose is the main energy source in the normal heart. However, fatty-acids are used as the only substrate available in the diabetic myocardium. Glucose is the main energy source in the normal heart. However, fatty-acids are used as the only substrate available in the diabetic myocardium.

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P1758 | BENCH
Favorable impact of pancreas transplant alone on left ventricular diastolic function and left ventricle mass in type 1 diabetes patients
L. Rondinini1, P. Giordano2, C. Alderighi1, E. Favilli1, N. Scelza1, L. Stazzoni1, M. Occhipinti2, U. Boggi2, P. Marchetti2, R. Mariotti1, R. Mariotti1
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Conclusion: Cardiac sympathetic innervation is more impaired in patients with IR and HF compared to matched non-IR patients. These findings contribute to explain the unfavorable prognostic impact of IR in patients with HF.
Conclusions: In a population of DM1 pts PTA (has) significantly improved LV diastolic Echo parameters and reduced LV mass indexes. Conversely, pts who did not receive PTA showed an increase in LV mass and wall thickness and a worsening trend in LV diastolic function.

P1754 | BEDSIDE
Impaired glucose metabolism as an independent risk for adverse cardiac events and progression of left ventricular diastolic dysfunction in dilated cardiomyopathy
Y. Ikeda, T. Inomata, Y. Iida, T. Nabeto, S. Ishi, T. Sato, T. Mizutani, T. Naruke, T. Koitabashi, J. Ako, Kitasato University School of Medicine, Cardiovascular Medicine, Sagamihara, Japan
Purpose: Although diabetes mellitus (DM) has been identified as a poor prognostic risk in heart failure (HF) patients, the association between DM and therapeutic response in patients with idiopathic dilated cardiomyopathy (IDCM) has not been clarified.
Methods: Among the 109 consecutive IDCM patients in 2007 - 2011, we reviewed the institutional records of 88 patients (81%) whose clinical data were available. Laboratory data analysis and serial echocardiography were performed at baseline and at 1 year follow-up. The patients were stratified into two groups on the basis of the presence of DM+ group (n=56) or absence of DM- group (n=52) of DM at baseline. Patients were followed up until death, cardiac events (CEs) such as major adverse cardiac events (MACEs), hospitalization for heart failure, or a reduction in cell shortening of rCM were assessed.
Results: Compared to controls, showing a median fluorescence intensity (mFI) for SA of 1.62 (1.52;1.72) a significant decrease by 17.4% in SA of DCM-IgG was measured at t0. Then, only IgG with NIA contained significantly less SA (1.28% vs. control). Interestingly, the inotropic activity of IgG correlated significantly with the amount of SA (r=0.8174). The amount of Gal in DCM-IgG was also significantly reduced by 26.9% vs. controls (mFI: 1.786 [1.6; 2.091]) but with a less pronounced correlation between the sugar content and the NIA of IgG (r=0.453). Six month post IA, we found a significant increase in the amount of SA in DCM-IgG to a level similar to that of controls (p<0.001). Here, DCM-IgG with the lowest levels of SA at t0 exhibited the highest percent increase of SA at t6m (r<0.0817). In consideration of the median increase, 87% of the DCM-IgG displaying a percent increase of Gal was <33%.
Conclusion: Our data reveal a link between the NIA of DCM-IgG on rCM and the diabetes salivation of these IgG. Moreover, since the strength of the NIA has been previously shown to be correlated with the improvement after IA, IgG-sialylation could be a predictor of the response to IA whereas IgG-galactosylation might be a marker for non-responder.

P1756 | BENCH
Diabetic hyperglycemia attenuates sympathetic dysfunction and oxidative stress after myocardial infarction in rats
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Previous research had demonstrated that hyperglycemia may protect the heart against ischemic injury. The aim of the study was to evaluate the participation of autonomic modulation and oxidative stress in diabetic hearts that had undergone 15 days of myocardial infarction. Male Wistar rats were divided into (n=8/group): control-sham (C), diabetes-sham (D), myocardial infarction (MI) and diabetes + myocardial infarction (DMI). Myocardial infarction was induced 15 days after diabetes induction by coronary occlusion. Cardiovascular autonomic modulation was evaluated by spectral analysis and oxidative stress profile was determined by: antioxidant enzymes activities, superoxide anion, protein carbonylation and redox balance of glutathione (GSH/GSSG) 15 days after MI and/or 30 days after diabetes induction (STZ, 50mg/kg). The diabetic and infarcted groups showed decrease in heart rate variability (p<0.05) and vagal modulation (p<0.05); however, the sympathetic modulation decreased only in diabetic groups (p<0.05). The cardiac redox status evaluated by GSH/GSSG ratio was lower in MI group (p<0.05). The diabetes induced increase in catalase concentration in D group (p<0.05). The glutathione peroxidase activity increased only in DMI group (p<0.05) The superoxide anion and protein carbonylation were increased only in MI group (p<0.05). The cardiac redox status evaluated by GSH/GSSG ratio was lower in MI group (p<0.05). In conclusion, these data suggest that hyperglycemia initiates compensatory mechanisms that could be protective to ischemia, as demonstrated by decreased sympathetic modulation, increased antioxidant enzymes and redox balance and reduction in protein carbonylation. These adaptations may be related with improvement in ventricular function and reduced infarcted area that was previously published in diabetic rats exposed to ischemic injury.

P1757 | BEDSIDE
Impact of diabetes mellitus on long-term prognosis in patients with preserved heart failure - a report from the Swedish Heart Failure Registry (S-HPR)
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Purpose: Patients with diabetes are at increased risk for developing heart failure.
We investigated the impact of diabetes on long-term prognosis in patients with heart failure and preserved left ventricular function from an everyday life perspective.

Methods: Patients with EF ≥50%, with (n=1658) and without (n=5047) type 2 diabetes included in the Swedish Heart Failure Registry (S-HFR) 2003-2011 were followed for mortality until 30 September 2011 (median 22.5 months). Differences in background characteristics were adjusted for in a logistic regression model.

Results: Patients with diabetes were younger (76 vs. 78 years), more often had known ischemic heart disease (47 vs. 36%), hypertension (68 vs. 52%), and more often had preserved renal function (eGFR >60 ml/min, 45 vs. 38%). NYHA class III and IV were somewhat more common in those with diabetes (44 vs. 39%). Kaplan-Meier curves for mortality are presented in Figure 1. The unadjusted and adjusted* ORs (95% CI) for mortality were 1.02 (0.92-1.15) and 1.39 (1.20-1.61).

Conclusion: Our data support that diabetes is an independent predictor of mortality in patients with preserved left ventricular function. As much as 50% of patients with preserved left ventricular function had reported ischemic heart disease, which questions the concept of a pure diabetic cardiomyopathy.

* Adjusted for gender, age, duration of heart failure, weight, blood pressure (systolic and diastolic), ischemic heart disease, hypertension, atrial fibrillation, pulmonary disease, revascularisation, eGFR class, Hb class, ACE inhibitors, ARBs, beta-blockers, mineralocorticoid receptor antagonists, diuretics, digitals, nitrates, statins and antiarrhythmic agents.

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P1759 | BEDSIDE
Comparison of the prognostic impact of diabetes mellitus between ischemic and non-ischemic heart failure -a report from the chart-2 study-

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Purpose: Diabetes mellitus (DM) is an important risk factor for mortality in patients with chronic heart failure (CHF). However, it is unclear whether the prognostic impact of DM differs between ischemic and non-ischemic heart failure (HF).

Methods: From our Chronic Heart Failure Analysis and Registry in our District-2 (CHART-2) Study (n=10,219), we enrolled 3,695 consecutive patients with symptomatic Stage C/D CHF patients (mean age 68.6 years, 68.8% male). We defined DM patients as those who had a history of DM treatment or had HbA1c ≥6.5% (NGSP) at the time of enrollment. Impacts of DM for the composite of death, myocardial infarction, stroke, and HF admission were examined in terms of ischemic and non-ischemic etiology of HF.

Results: During the median follow-up of 3.0 years, there were 952 composite events (25.8%). The prevalence of DM was significantly higher in ischemic HF (863/1,767, 48.8%) than in non-ischemic HF (627/1,928, 32.5%) (P=0.001). Ischemic HF patients were characterized by older age and more male gender, and lower brain natriuretic peptide level as compared with non-ischemic HF patients. DM patients were characterized by younger age, higher body mass index, and higher prevalence of renal dysfunction in both groups. Kaplan-Meier curves showed that DM had a significant prognostic impact in ischemic HF but not in non-ischemic HF (Figure). Multivariate adjusted Cox analysis further demonstrated that DM was significantly associated with composite endpoints in ischemic HF (adjusted hazard ratio (HR) 1.33, P=0.004), but not in non-ischemic HF (adjusted HR 1.07, P=0.49) (P for interaction=0.81).

Conclusions: These results indicate that the prognostic impact of DM was more evident in ischemic HF than in non-ischemic HF.

HEART FAILURE MANAGEMENT II

P1761 | BENCH
Effect of cardiac resynchronization therapy on clinical course of ventricular tachycardias in patients with dilated cardiomyopathy and severe heart failure


Purpose: To evaluate the effect of cardiac resynchronization therapy (CRT) on clinical course of ventricular tachycardias in patients with dilated cardiomyopathy (DCM).

Materials and methods: The study included a total of 70 patients with DCM aged 32 to 75 years (55±12 years). All patients had NYHA functional class (FC) III heart failure (HF) with left ventricular (LV) ejection fraction (EF) of 30.1±3.8%, 6-minute walk test distance of 290.5±64.3 m, and LV end diastolic volume (EDV) of 225±150 mL. Before CRT device implantation and 1 year after it, all patients received 24-hour ECG monitoring. Patients were assigned to groups according to the registration of ventricular tachycardia (VT) paroxysms. Group 1 included 35 patients (50%) with diagnosed VT paroxysms occurring in the presence of adequate doses of antiarrhythmics. Group 2 included 35 patients (50%) without registered VT episodes. Before CRT, all patients received equilibrium radionucleide ventriculography (ERVG) with evaluation of LV EF improvement. All patients received implantation of CRT devices with defibrillator function.

Results: One year after beginning of CRT, all patients showed clinical improvement: LV EF increased from 30.1±3.8% to 42.8±4.8% (p<0.001); NYHA HF FC changed from III to II; 6-minute walk test distance increased from 290.5±64.3 m to 377.2±45.3 m (p<0.001); and LV EDV decreased from 220.7±50.9 mL to 185.7±49.2 mL. GLS was a all-cause mortality.

Conclusions: GLS is an independent predictor of both CV and all-cause mortality in the AdvCKD and is more sensitive discriminator than EF for determining LV dysfunction in this cohort.
Aim: To evaluate the effectiveness of treatment guided by the new Li device with patients of CHF. Methods and results: We have shown previously that an Li decrease of more than 24% from dry (baseline) Li reflects the clinical threshold of lung fluid accumulation to PCE and hospitalization by > 95% probability. We recruited 222 patients during the first month after hospitalization for PCE (age 67±11 years, male 85%, LVEF 26±7%) at NYHA II/III/IV (97/86/39, respectively) and followed them in an outpatient clinic for 32±21 months on a monthly basis. Initial NT-proBNP level was 3771±5185 pg/ml. Patients were randomized (1:1) into 2 well-matched groups according to treatment policy. Group 1 included patients treated according to measured Li while group 2 patients were treated by clinical assessment alone. There were 16 cardiovascular deaths and 5 non-cardiovascular deaths in group 1 and 30 and 6 in group 2, respectively (p=0.006). The annual number hospitalizations for PCE in groups 1 and 2 were 70 and 139, respectively (p<0.001). In patients whose treatment was Li-guided (group 1) preemptive therapy was intensified 3 times more frequently than in group 2 (p<0.001). The annual non PCE hospitalizations were 74 and 85 in group 1 and 2, respectively (NS).

Conclusion: Guided treatment in CHF patients reduced recurrent hospitalizations due to PCE and improved survival.

P1764 | BEDSIDE Could the presence of depressive symptoms affect the results of exercise testing in men with systolic heart failure? E. Kalicinska1, K. Wojtas1, M. Drozd2, K. Wegrzynowska-Teodorczyk3, J. Majda4, W. Banasiak1, P. Ponikowski1, E.A. Jankowska2. 1Centre for Heart Diseases, Military Hospital, Wroclaw, 2Lab. for Applied Research on Cardiovascular System, Dept. of Heart Diseases, Medical University, Wroclaw, Poland

Background: Exercise intolerance is one of the most important symptoms in heart failure (HF). It can be assessed using the cardiopulmonary exercise testing (CPX) with the assessment of peak oxygen consumption (peak VO2) and ventilatory response to exercise (VE-VCO2 slope) as well as a distance of 6-minute walk test (6-MWT). There are premises that the presence of depressive symptoms may affect the results of exercise testing, however, this issue has never been tested in patients with systolic HF.

Methods: We examined 197 men with systolic HF (mean age: 60±11 years, EF mean: 32±13%). Subjects were divided into three groups based on left ventricular dysfunction III–IV: 58%, ischaemic aetiology: 66%, mean LVEF: 31±7%). At the initial stages of decompensation, patients have neither signs of congestion nor severe dyspnoea. At the late stages of decompensation patients have both signs of congestion and severe dyspnoea. One of the strategies used in decompensation is preemptive therapy which is indicated to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity. Coexistence of depressive symptoms and poor 6-MWT performance. Somatic depressive symptoms were strongly related to all measures of exercise capacity.

Results: In men with systolic HF, mean peak VO2 was 15.9±4.8 ml/min/kg (peak VO2: <14 ml/min/kg was present in 33.5% of pts), median VE-VCO2 slope was 33.6 (28.8±4.3) (VE-VCO2 slope:34 was present in approx. 50% of pts), and 6-MWT distance was 473±118 m (6-MWT distance: <450 m was present in 36% of pts). Patients with reduced peak VO2 had more intense somatic and cognitive depressive symptoms (10.5±8.5 and 7.7±7.7) than patients with peak VO2>14 ml/min/kg (6±3.8 and 4±3.8) (all p<0.0001). Patients with VE-VCO2 slope>34 had more intense somatic and cognitive depressive symptoms (9±5 and 6±6) than patients with VE-VCO2 slope<34 (6.4±4.6 and 6.4±4.7) (p<0.0001 and p=0.01, respectively). Patients with 6-MWT distance<450 m had more intense somatic and cognitive depressive symptoms (12±5 and 8±7) than patients with 6-MWT distance≥450 (8.5±4 and 4±4) (all p<0.0001).

Conclusions: Patients with worse exercise performance had more pronounced overall depressive symptoms, particularly with somatic one (b=0.33, p<0.0001). Poor performance of 6-MWT was strongly associated with more pronounced all depressive symptoms particularly with somatic one (b=0.26, p<0.0001). Higher VE-VCO2 slope was strongly associated only with more severe somatic depressive symptoms (b=0.24, p<0.0001). Patients with worse exercise performance had more pronounced all depressive symptoms particularly with somatic one (b=0.26, p<0.0001). Higher VE-VCO2 slope was strongly associated only with more severe somatic depressive symptoms (b=0.24, p<0.0001). Patients with worse exercise performance had more pronounced all depressive symptoms particularly with somatic one (b=0.26, p<0.0001). Higher VE-VCO2 slope was strongly associated only with more severe somatic depressive symptoms (b=0.24, p<0.0001). Patients with worse exercise performance had more pronounced all depressive symptoms particularly with somatic one (b=0.26, p<0.0001). Higher VE-VCO2 slope was strongly associated only with more severe somatic depressive symptoms (b=0.24, p<0.0001). Patients with worse exercise performance had more pronounced all depressive symptoms particularly with somatic one (b=0.26, p<0.0001).

P1765 | BEDSIDE Non-adherence to recommended therapy as a cause of heart failure decompensation R. Pelocho1, J. Ceral1, V. Vorisek2, V. Furmanova2, M. Solar1. 1Charles University - Faculty of Medicine Hradec Kralove, University Hospital Hradec Kralove, 1st Dept. of Internal Medicine – Cardiology, Hradec Kralove, 2Charles University - Faculty of Medicine Hradec Kralove, University Hospital Hradec Kralove, Institute of Clinical Biochemistry and Diagnostics, Hradec Kralove, Czech Republic

Purpose: The cause of acute heart failure decompensation is frequently unknown. The non-adherence to the prescribed medication may be present in some individuals. The goal of the study is to assess the frequency of non-adherence to the recommended therapy in patients with acutely decompenated chronic heart failure.

Methods: Serum levels of prescribed medications were used as an indicator of drug adherence. Serum drug levels (SDLs) were evaluated by liquid chromatography and mass spectrometry. The chromatographic separation was performed on a C18 column with mobile phase consisting of N,N-diisopropylethylamine and 0.1% trifluoroacetic acid in the mobile phase. The detection of analyzed substances was accomplished on a linear ion-trap mass spectrometer. The subjects were labeled as non-adherent when the serum level of at least one of the evaluated drugs was below the limit of quantification. The results of
SDs had no influence on the clinical evaluation and acute management of the enrolled patients.

Results: The study assessed the data of 50 patients with acutely decompensated chronic heart failure. The main underlying causes of chronic heart failure were: coronary artery disease (14, 28%), combination of coronary artery disease and significant valvular heart disease (14, 28%), cardiomyopathy (8, 16%) and severe valvular heart disease (6, 12%). The acute decompensation of heart failure was caused by acute coronary syndrome (5, 10%), infection (5, 10%), arrhythmia (2, 4%), anemia (1, 2%), uncontrolled arterial hypertension (1, 2%), and progres- sive systolic valve heart disease (1, 2%). Three (6%) patients conceded omission of recommended medication, and in one individual (2%) the medication was inappropriately changed by the attending physician. In 31 patients (62%) the cause of acute cardiac decompensation remained unclear based on routine clinical exams performed. Among the evaluated drugs were determined in the sera of 28 (56%) study patients. The non-adherence was diagnosed in the remaining 22 (44%) patients. None of prescribed drugs was found in the sera of 5 (10%) patients. In patients with unknown precipitating cause of heart failure decompensation (31), the non-adherence was diagnosed in 13 (42%), none of prescribed drugs was detected with unknown precipitating cause of heart failure decompensation (31), the non-adherence was diagnosed in the remaining 22 (44%) patients.

Conclusion: Our data suggest that the non-adherence to the recommended ther- apy may be a significant cause of acute decompensation of chronic heart failure. The assessment of serum drug levels may be used for this purpose.

P1767 | BEDSIDE
Carbon monoxide intoxication induced left ventricular dysfunction

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Purpose: Carbon monoxide (CO) intoxication could cause significant cardiac in- jury. Cardiac dysfunction after CO intoxication can be presented as various clinical patterns. The echocardiographic findings after CO intoxication are poorly defined. The purpose of this study was to evaluate the clinical patterns of left ventricular (LV) dysfunction using echocardiography.

Methods: One-hundred thirty two CO intoxicated patients (81 males, 46 females) were included. Clinical, demographic and labora- tory data and transthoracic echocardiographic findings were analyzed.

Results: Left ventricular dysfunction developed in 29 patients (15 males, 47 ± 20 years old). The LV dysfunction group showed higher lactate level (5.8 ± 3.3 vs. 4.1 ± 3.5 mmol/L, p < 0.024) and lower base excess (-8.2 ± 6.0 vs. -4.8 ± 4.7 mEq/L, p < 0.001) compared with normal LV function group. Among the LV dysfunction group, 3 different echocardiographic patterns were presented (Table). Regional wall motion abnormality (RWMA) was presented in 14 patients. Akoesia of the mid and apical segments of LV with sparing of the basal segments, typical finding of Takotsubo cardiomyopathy, was presented in 8 patients. Global hypokinesia of LV was presented in 7 patients.

Table 1. Pattern of LV dysfunction

<table>
<thead>
<tr>
<th>RWMA group</th>
<th>Takotsubo type CMP group</th>
<th>Global HK group</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>(n=14)</td>
<td>(n=8)</td>
<td>(n=7)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>51±21</td>
<td>44±23</td>
<td>44±16</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>7 (50%)</td>
<td>13 (113%)</td>
<td>7 (100%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27±5.6</td>
<td>21±6.9</td>
<td>26±11.1</td>
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<tr>
<td>AST (U/L)</td>
<td>67±35.4</td>
<td>54±62.2</td>
<td>809±1000.5</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>5.3±2.8</td>
<td>4.3±2.4</td>
<td>8.4±2.4</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>46±12.3</td>
<td>26.8±49.1</td>
<td>177±227.3</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>141±9.6</td>
<td>20.3±16.7</td>
<td>123±11.9</td>
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<tr>
<td>EF (%)</td>
<td>43±15.6</td>
<td>37±10.3</td>
<td>36±4.15</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.5±0.5</td>
<td>1.9±2.4</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusions: Our results demonstrate that CO intoxication could induce various patterns of LV dysfunction.

P1768 | BEDSIDE
Urine uric acid level in spot sample on admission is useful as a predictive marker for in-hospital renal failure

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Purpose: We examined whether a spot urine analysis on admission can be useful as a new predictive marker for in-hospital renal failure in patients with ADHF.

Method: A total of 280 consecutive ADHF patients who admitted to our institu- tion between January 2013 and December 2013 from prospective registry was studied. Of them, 258 patients, who underwent urinalysis within 48 hours of admission, were included. In-hospital renal failure was defined as the increase in more than 25% or 0.3 mg/dL of serum creatinine.

Result: In-hospital renal failure was seen in 50 patients (19%), 15 of whom experienced by 48 hours of admission. Patients with in-hospital renal dysfunction, compared with those without, were older, had higher serum creati- nine (sCr), HbA1c, and eGFR levels, severer mitral regurgitation by echocardio- graphy, and was more frequently treated with dobutamine, PDEIII inhibitor and nitrroglycerin. On the other hand, the creatinine (uCr), uric acid (uUA), urine urea nitrogen (uUN), serum uric acid (sUA)/uUA ratio, urine potassium/serum potassium ratio, uUA/uCr ratio, urinary nomaisty, and plasma osmolality were significantly lower in patients with in-hospital renal dysfunction than those without. According to univariate analysis, uUA/uCr and sUA were the strongest predictors (p < 0.01, OR=1.25) in all parameters.

Conclusions: Urinary uric acid level in spot sample divided by serum uric acid level can strongly predict in-hospital renal dysfunction in patients admitted with ADHF.

P1769 | BENCH
Non-invasive monitoring of lung impedance in chronic heart failure patients

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Background: Prevention of hospitalizations for decompensation in Chronic Heart Failure (CHF) patients is an unresolved issue. The accuracy of existing devices in predicting deteriorating is only 38-76%.

Aim: We evaluated the ability of the new a non-invasive method for lung impedance monitoring to predict decompensation in CHF patients.

Methods: Monitoring CHF patients was accomplished by a device which mea- sures "net" lung impedance (LI) instead of traditionally used transthoracic impedance monitoring to predict decompensation in CHF patients.

Results: A total of 280 consecutive ADHF patients who admitted to our institu- tion were recruited after index hospitalization for acute heart failure (AHF) and followed in an outpatient clinic for 32±11 years. The UN (sUN)/uUN ratio, urine potassium/serum potassium ratio, uUA/uCr ratio, urinary nomaisty, and plasma osmolality were significantly lower in patients with in-hospital renal dysfunction than those without. According to univariate analysis, uUA/uCr was the strongest predictor (p < 0.01, OR=1.25) in all parameters.
P1770 | BENCH
Persistent long-term apparent healing in a large cohort of patients with idiopathic dilated cardiomyopathy: prevalence and characterization
M. Merlo1, D. Stolfo1, M. Anzini1, F. Negrini2, G.A. D'angelo1, B. Pinamonti1, G. Barbati1, A. Di Lenarda2, G. Sinagoga1, 1University Hospital “Ospedali Riuniti”, Cardiovascular Department, Trieste, Italy; 2Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy
Background: Data regarding the characterization and prognostic role of persistent long-term apparent healing in large populations of patients with idiopathic dilated cardiomyopathy (IDCM) are lacking.
Methods and results: We analyzed 431 IDCM patients (potential follow-up: at least 8 years; mean follow-up: 180±56 months) receiving tailored medical treatment. Apparent healing was defined as: left ventricular ejection fraction (LVEF) ≥50% and indexed left ventricular end-diastolic diameter (LVEDD) ≤33 mm²/m² at mid-term follow-up (19±4 months). Apparent healing was considered persistent when the above-mentioned parameters were maintained at long-term (103±5 months). At mid-term 86/431 (20%) patients were apparently healed; 60% of them showed a persistent apparent healing. No baseline and mid-term predictors of persistent apparent healing were found. In persistently apparently healed patients all main clinical/laboratory parameters reached the normalization at 90% specificity otherwise maintained it; conversely, in non-persistently apparently healed patients the parameters progressively worsened after the 5th year of follow-up despite their mid-term normalization. During the very-long-term follow-up, persistently apparently healed patients showed a better heart transplant-free survival (95 vs. 71%, p=0.014) and fewer devices implantations (5 vs 24%) with respect to non-persistently apparently healed patients.
Conclusions: Persistent long-term apparent healing was evident in a remarkable proportion of IDCM patients receiving optimal medical treatment and was associated with stable normalization of main clinical/laboratory features and with excellent very-long-term survival. However no early predictors of this condition were found, highlighting the relevance of a continuous and individualized follow-up in this scenario.

P1771 | BENCH
Chronic levosimendan treatment improves functional capacity of the hypertrophic and failing right heart
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Purpose: To investigate if chronic treatment with levosimendan can prevent and reverse pressure overload induced right ventricular hypertrophy and failure in rats.
Methods: Right ventricular hypertrophy and failure was induced in male Wistar rat weanlings (77±6 g) by pulmonary trunk banding (PTB) with a titanium clip compressed to an inner diameter of 0.6 mm. A control group was sham operated. Rats were randomized to treatment with vehicle (n=10, VEH), levosimendan (3 mg/kg/day) three weeks after surgery (n=10, REV), Sham operated rats received vehicle treatment (n=16, SHAM). Right ventricular function was evaluated at the end of study, seven weeks after surgery, by high frequency echocardiography, magnetic resonance imaging, pressure volume relations, and gross anatomy.
Results: Pulmonary trunk banding induced right ventricular hypertrophy with compensated heart failure evident by a decrease in cardiac output and the absence of extra-cardiac manifestations of heart failure. Levosimendan treatment prevented and reverted deterioration of right ventricular function measured by cardiac index (Fig. 1). Deterioration of right ventricular function was prevented by levosimendan treatment measured by ejection fraction (EF) and by the load-independent measure of systolic function: end systolic elastance (Ees) (EF: VEH vs. PREV 57% ± 2% vs. 68% ± 3%, p<0.01; Ees: VEH vs. PREV 367 ± 57 vs. 667±118 mm Hg/ml, p<0.05), but only a trend towards normalization was observed using the reversal strategy.
Conclusion: Chronic treatment with levosimendan completely prevents the development of right ventricular failure and partially reverts established right ventricular failure induced by chronic pressure overload.

UNDERSTANDING HEART FAILURE WITH PRESERVED EJECTION FRACTION
P1773 | BEDSIDE
Noninvasive estimation of left ventricular filling pressures during exercise in patients with preserved left ventricular ejection fraction: comparative study, catheterization versus echocardiography
Background: Latent heart failure at rest could be revealed in a number of patients upon exercise. The noninvasive diagnosis of this condition remain challenging.

P1774 | BEDSIDE
Pulmonary vascular response assessment in heart failure with preserved ejection fraction and pulmonary hypertension
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Purpose: Pulmonary vascular response patterns to exercise have not been studied extensively in symptomatic heart failure with reduced ejection fraction (HF/EF) and pulmonary hypertension (PH).
Methods: Consecutive, symptomatic HF/EF patients (n=40), with mean pulmonary arterial pressure (MPAP) ≤25 mmHg, pulmonary capillary wedge pressure (PCWP) >15 mmHg, and cardiac index ≥2.5 L/min/m², received protocol-driven, titrated sodium nitroprusside (SNP) and diuretics until mean arterial pressure (20±2 mmHg) was achieved. Pulmonary arterial pressure (MPAP) with MPAP >25 mmHg indicating a high risk zone for rehospitalization for AHF with 100% sensitivity and 90% specificity. Changes and intensification of therapy is mandatory when MPAP decreases by more than 24%.

Conclusions: Noninvasive "net" LI monitoring is a very sensitive method to predict hospitalization for exacerbation of CHF. LI decreased by >24% from baseline represents a high risk zone for re-hospitalization for AHF with 100% sensitivity and 90% specificity. Changes and intensification of therapy is mandatory when LI decreases by more than 24%.
Cardiac dysfunction associated with acute brain hemorrhage

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Purpose: Cardiac dysfunction associated with brain hemorrhage was not well studied. We evaluated the incidence and characteristics of acute cardiac dysfunction related with acute brain hemorrhage.

Methods: Between January and September in 2013, consecutive patients who were admitted to the hospital or were admitted to the surgical ICU were prospectively enrolled. ECG, cardiac enzyme, and echocardiography were performed in all patients. Left ventricular (LV) systolic dysfunction observed on echocardiography was considered as acute cardiac dysfunction related with brain hemorrhage when all the following criteria were satisfied: (1) accompanied ECG change and abnormal cardiac enzyme level, (2) no previous history of cardiac disease, and (3) regional wall motion abnormality (RWMA) extending beyond a single coronary arterial distribution. Otherwise, LV dysfunction was considered as cardiac dysfunction not related with brain hemorrhage. Clinical characteristics, laboratory findings, and in-hospital outcome were retrospectively reviewed.

Results: Total of 107 patients (age: 59±16 years, 64 men) were collected. LV systolic dysfunction on echocardiography was observed in 18 (17%) patients. Among them 11 (10%) patients were classified as having acute cardiac dysfunction related with brain hemorrhage. While 5 patients in 11 patients with acute cardiac dysfunction showed typical apical ballooning, 6 patients showed inverted takotsubo pattern. Other abnormalities were observed in ECG, cardiac enzyme level and echocardiography were shown in the table. In-hospital mortality was observed in 19 (18%) patients. Six patients in 11 patients with acute cardiac dysfunction had in-hospital mortality (p<0.004).

Conclusion: Acute cardiac dysfunction associated with acute brain hemorrhage was observed in 10% of patients and half of them showed inverted takotsubo pattern.

Treated with Nebivolol: data from SENIORS trial

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Purpose: There is limited information about the effects of beta-blockers in HF stratified by blood pressure especially in the elderly and those with preserved ejection fraction (EF). We evaluate the effects of nebivolol on the composite outcome of all-cause mortality or cardiovascular hospitalization in elderly patients with HF stratified by SBP and EF.

Methods and results: The SENIORS trial evaluated the effects of nebivolol and enrolled 2128 patients >70 years with HF. Patients were divided into 2 SBP categories (<120 mmHg and ≥120 mmHg) and 2 EF categories (<40% and ≥40%). Mean age was 76 years, 37% were female, mean ejection fraction 36%. Low baseline SBP was associated with worse clinical outcomes irrespective of treatment group, both in patients with reduced and preserved EF. When stratified by SBP and EF no difference was found in numerically more beneficial placebo in all analyses; however, this was not statistically significant. There was a similar effect in patients with reduced and preserved EF (Table 1).

Table 1. Effect of treatment according to blood pressure and ejection fraction

<table>
<thead>
<tr>
<th>SBP category</th>
<th>Events per 1,000 years ratio</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p value</th>
<th>Interaction p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;120 mmHg</td>
<td>338.9</td>
<td>270.0</td>
<td>0.81</td>
<td>0.59-1.12</td>
<td>0.20</td>
</tr>
<tr>
<td>≥120 mmHg</td>
<td>223.4</td>
<td>195.8</td>
<td>0.88</td>
<td>0.71-1.08</td>
<td>0.18</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;120 mmHg</td>
<td>37.74</td>
<td>198.7</td>
<td>0.52</td>
<td>0.25-1.09</td>
<td>0.08</td>
</tr>
<tr>
<td>≥120 mmHg</td>
<td>201.5</td>
<td>174.2</td>
<td>0.87</td>
<td>0.64-1.17</td>
<td>0.34</td>
</tr>
</tbody>
</table>

Conclusion: Elderly HF patients with lower SBP have a worse outcome than those with higher SBP but nebivolol appears to be safe and well tolerated with similar effect on the composite outcome of death or CV hospital admission irrespective of baseline SBP and LVEF.

Prognostic significance and determinants of the 6-minute walk test in patients with pulmonary hypertension associated with heart failure and preserved ejection fraction

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1Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; 2Medical University of Vienna, Division of Dermatology, Vienna, Austria

Background: Symptoms of exertional fatigue and dyspnea, as well as a reduced
exercise tolerance are cardinal features of pulmonary hypertension (PH) associated with heart failure with preserved ejection fraction (HFpEF). The underlying mechanisms limiting exercise capacity in this complex clinical syndrome remain incompletely understood. The aim of the present study was to define the prognostic significance and clinical determinants of the six-minute walking distance (6-MWD).

Methods: Consecutive patients with a definite diagnosis of PH-HFpEF as confirmed by right heart catheter, were enrolled in our prospective, observational registry. Hospitalization for HF and/or death for cardiac reason were defined as the primary study endpoint. To establish determinants of the 6-MWD, four separate multiple regression models were constructed for TTE, hemodynamic, laboratory and pulmonary parameters. For quantification of left ventricular (LV) extracellular matrix (ECM) using the TissueFAXS and HistoQuest® software, myocardial biopsies were taken from 18 patients.

Results: Between December 2010 and July 2013, 142 PH-HFpEF patients (99 women and 43 men, mean age 71±9 years) were included to the study. After a mean follow-up of 14.0±10.0 months (range 0.5 – 34.0 months), 43 patients (30.3%) reached the combined endpoint. Patients in the adverse outcome group had a significantly shorter 6-MWD (246.8±115.6 m versus 345±110.2 m, P<0.001) and a higher Borg dyspnea score (BDS; 5±2 versus 3±1, P<0.001). The 6-MWD (hazard ratio [HR]; 0.992; 95% confidence interval [CI]; 0.990; 0.995; P=0.013) was found to be an independent predictor of outcome. Other clinical parameters associated with 6-MWD were presence of atrial fibrillation (HR: 2.482; 95%CI: 1.198; 5.139, P=0.014) and COPD (HR: 2.048; 95%CI: 1.084; 3.869; P=0.039). The following parameters were found to be independent determinants of the 6-MWD: systolic and mean pulmonary artery pressures, transpulmonary gradient, pulmonary arterial compliance, hemoglobin, urea, partial pressure of carbon dioxide in arterial blood and vital capacity. There was a significant inverse correlation between the 6-MWD and the amount of ECM (R=−0.501, P=0.034) in the heart tissue samples.

Discussion: The limited exercise capacity in PH-HFpEF patients can be explained by a variety of cardiac and non-cardiac factors that contribute to increased ECM deposition in the LV and consecutive hemodynamic alterations. We hypothesize that PH-HFpEF is a multifactorial systemic disease with end-organ damage of the heart.

P1779 | BEDSIDE
A biomarker for diastolic heart failure
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M. Raicu2, D. Zhang2, T. Toreş2, P1779 | BEDSIDE
P1781 | BEDSIDE
P1782 | BEDSIDE
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Purpose: MicroRNAs (miRs) are essential regulators of gene expression implicated in cardiovascular function and disease. MiR-21 and miR-133 have been shown to play a role in heart hypertrophy and fibrosis. They have also been shown to regulate proliferation and phenotypic switch of vascular smooth muscle cells. However, there are limited data regarding their role in left ventricular (LV) diastolic dysfunction. The aim of this study is to investigate miR-21 and miR-133 levels in peripheral blood mononuclear cells in patients with heart failure with preserved ejection fraction (HFpEF).

Methods: We included 33 patients with symptoms and signs of heart failure who had an LVEF >50% and evidence of LV diastolic dysfunction (19 males, aged 58±10 years. Blood samples were also obtained from 29 healthy volunteers for comparison (17 males, aged 56±8 years). All subjects underwent a complete echocardiographic study. Peripheral blood mononuclear cells (PBMCs) were isolated and microRNA levels were determined by quantitative real time reverse transcription PCR. Results: MiR-21 levels were found to be higher (3.6±0.41 versus 2.05±0.31, p<0.05) while miR-133 levels were found to be lower (11.26±4.9 versus 37.03±8.18, p<0.05) in patients with LV diastolic dysfunction compared to healthy controls. MiR-21 levels showed strong negative correlations with E′ (r=−0.42, p<0.01) while miR-133 levels showed strong positive correlations with E′ (r=0.40, p<0.001).

Conclusions: Patients with LV diastolic dysfunction were shown to have a strong relationship with miR-21 and miR-133 levels in peripheral blood mononuclear cells. Our findings contribute to the understanding of pathogenesis of HFpEF and might offer a new therapeutic target.

P1780
Soluble ST2 is associated with markers of diastolic heart failure in patients with heart failure with preserved ejection fraction in the PARAMOUNT trial
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Background: The cardiac fibrosis marker ST2 is associated with severity of heart failure and adverse prognosis in heart failure with reduced ejection fraction. The association between ST2 and clinical characteristics or measures of cardiac structure and function in patients with heart failure with preserved ejection fraction (HFpEF) is unclear.

Methods: We studied 296 patients from the Prospective comparison of ARNI with ARB on Management Of heart failure with preserved ejection fraction (PARAMOUNT) trial with a measurement of ST2. We related ST2 levels to baseline clinical and echocardiographic characteristics.

Results: The cardiac fibrosis marker ST2 is associated with severity of heart failure and adverse prognosis in heart failure with reduced ejection fraction. The association between ST2 and clinical characteristics or measures of cardiac structure and function in patients with heart failure with preserved ejection fraction (HFpEF) is unclear.
line characteristics and echocardiographic measures and assessed the effect of randomized therapy at 36 weeks.

**Results:** The median ST2 level was 33.1 ng/mL (IQR 24.6-48.1). Higher ST2 was associated with older age, male sex, atrial fibrillation, higher NYHA class, higher NT-proBNP and lower eGFR (Table). Increasing ST2 levels were associated with higher E/E’ and larger left atrial size (Table). Associations were similar after excluding patients with atrial fibrillation. In a multivariable model male sex, increasing NYHA class and left atrial volume were independently associated with higher ST2. Treatment with LCZ696 did not reduce ST2 levels at 12 (p=0.97) or 36 weeks (p=0.76).

**Characteristics by ST2 quartiles**

<table>
<thead>
<tr>
<th>Quartile</th>
<th>n=74</th>
<th>n=74</th>
<th>n=74</th>
<th>n=74</th>
<th>n=74</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>69±10</td>
<td>70±10</td>
<td>71±8</td>
<td>74±8</td>
<td>0.02</td>
</tr>
<tr>
<td>Women (%)</td>
<td>47 (64%)</td>
<td>45 (61%)</td>
<td>38 (51%)</td>
<td>36 (49%)</td>
<td>0.04</td>
</tr>
<tr>
<td>AF (%)</td>
<td>17 (23%)</td>
<td>32 (43%)</td>
<td>33 (45%)</td>
<td>39 (53%)</td>
<td>0.001</td>
</tr>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>774</td>
<td>716</td>
<td>957</td>
<td>1014</td>
<td>0.002</td>
</tr>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>774</td>
<td>716</td>
<td>957</td>
<td>1014</td>
<td>0.002</td>
</tr>
<tr>
<td>eGFR (mL/min per 1.73 m²)</td>
<td>69±21</td>
<td>68±20</td>
<td>62±21</td>
<td>61±18</td>
<td>0.005</td>
</tr>
<tr>
<td>E/E’</td>
<td>10.9±3.9</td>
<td>13.6±6.0</td>
<td>13.3±6.9</td>
<td>13.7±6.6</td>
<td>0.02</td>
</tr>
<tr>
<td>LA volume index (m²/m²)</td>
<td>32±12</td>
<td>35±13</td>
<td>36±14</td>
<td>40±15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AF, atrial fibrillation; LA, left atrial; eGFR, estimated glomerular filtration rate.</td>
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<td></td>
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</tbody>
</table>

**Conclusion:** Our findings suggest that ST2 is associated with markers of wall stress and diastolic dysfunction in HfPEF. Whether ST2 represents simply a biomarker associated with disease severity in HfPEF or contributes to the pathogenesis remains unclear.

### P1783 | BEDSIDE

**Evolution of left ventricular function by speckle tracking ecoangiography in heart transplanted patients**


**Introduction:** Although ejection fraction (EF) is usually normal after heart transplantation (HT), regional systolic function can be impaired. Strain is an accurate tool for assessment of myocardial function in this patients. **Objective:** To compare left ventricular function in HT patients with healthy controls in the first two years after HT. **Methods:** We included 29 HT patients followed over one year, 20 of them completed two years, and 13 healthy controls. Studies with endomyocardial biopsy rejection ≥2R were excluded. EF by biplane Simpsons method and interventricular septum thickness were determined. LV global longitudinal strain (GLS) by Speckle Tracking technique was measured in 12 LV segments in 4 and 2 chambers view.

**Results:** Our results are shown in the table below.

**Evolution of LV function**

<table>
<thead>
<tr>
<th>IVST (n=74)</th>
<th>EF (n=74)</th>
<th>Global GLS (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>9.4±1.8</td>
<td>62.2±5.2</td>
</tr>
<tr>
<td>1 year</td>
<td>10.6±1.2</td>
<td>63.5±5.0</td>
</tr>
<tr>
<td>2 years</td>
<td>11.2±1.1</td>
<td>64.1±7.1</td>
</tr>
</tbody>
</table>

*p<0.01 compared to controls. Global GLS: global LV longitudinal strain.**

**Conclusions:** Despite normal EF in HT patients, LV GLS values were significantly reduced compared to healthy controls in the first month after transplantation, so these reduced parameters may be interpreted as “normal” strain values in “healthy” transplant patients. They improved progressively until complete normalization after two years follow up. This is the first study to show a full recovery in LV function by Speckle-tracking technique.

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### YOUNG INVESTIGATORS AWARDS SESSION: CLINICAL SCIENCE

#### 1784 | BEDSIDE

**Intracoronary autologous cardiac progenitor cell transfer in children with hypoplastic left heart syndrome 2-year results of the TICAP trial**

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**Background:** Hypoplastic left heart syndrome (HLHS) is one of the most high-risk conditions in children with congenital heart disease. Objective: The aim of this study is to determine whether intracoronary delivery of autologous cardiophere-derived cells (CDCs) was feasible and safe to treat the children with HLHS. **Methods and design:** This phase-1 trial (TICAP: NCT01273857) is a prospective controlled exploratory study. Four-teen patients with HLHS who are undergoing staged-2 or -3 surgical palliations were enrolled between January, 2011, and January, 2012. Seven patients constitutively assigned to receive intracoronary single-dose injection of CDCs 1 month after the surgical palliations followed with hypoplastic heart patients allocated to a control group with standard care alone. The primary endpoint was to assess the safety and the secondary endpoint was the preliminary efficacy to verify the improvements of the right ventricular function as well as the clinical symptoms of heart failure status and 2 scores for weight-for-age from baseline (1 month after surgical palliations) to 3, 12, and 24 months of follow-up. **Results:** No complications, including cardiac death, myocardial ischemia, proarrhythmia, hospitalization for heart failure, and tumor formation, were reported within first months of CDC infusion. Ecoangiography showed that improvement of right ventricular ejection fraction (RVEF) was greater in the CDC-treated group (+5.3±3.2%) than in controls (+0.1±3.4%, P=0.01) at 3 months after CDC infusion. This cardiac function enhancement was manifested even 1 year and 2 years after CDC infusion (+7.8±4.9% vs. +2.2±3.1% at 1 year, P=0.03; +8.6±3.7% vs. +3.4±6.4% at 2 years, P=0.04). In addition, RVEF measured by CMRI was also markedly improved in CDC-treated patients from 36.1±7.5% at baseline to 42.7±8.7% at 1 year (P=0.04) and to 44.7±7.7% at 2 years (P=0.047). No statistically significant changes in clinical symptoms of heart failure status were observed. Also, all of these parameters did not change in control subjects. **Conclusion:** These encouraging results of 2-year follow-up of TICAP trial suggest that intracoronary infusion of autologous CDCs is feasible and safe to treat the children with HLHS. This novel therapeutic strategy may impact on cardiac function as well as clinical symptom of heart failure status and somatic growth in long-term outcome.

#### 1785 | BEDSIDE

**Performance of novel adenosine-free and established indices of coronary lesion severity using invasive and non-invasive techniques, as well as absolute quantification of myocardial blood flow**

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**Purpose:** Ischaemia guided therapy of coronary artery disease with the use of Fractional Flow Reserve (FFR) has been shown to improve patient outcomes. Recent work has proposed the instantaneous wave-free ratio (iFR) and Basal Stenosis Resistance (BSR) as novel adenosine-free techniques to assess stenosis severity equivalent to FFR. The diagnostic performance of these new compared to more established tests is not clear, limited by the lack of a true gold-standard test for coronary ischaemia. We aimed to investigate these processes by developing a model of coronary ischaemia with invasive, non-invasive and ex-vivo applications. **Methods:** A model of coronary stenosis was developed in anaesthetised Lan- caster pigs, for invasive assessment of coronary haemodynamics, adenosine stress perfusion MRI (CMR), and microsphere quantification of absolute myocardial blood flow (MBF). Lesions were created using an adjustable external balloon constrictor, via a mini-thoracotomy. An intracoronary wire distal to the stenosis measured pressure and flow velocity at rest and adenosine-induced hyperemia. Perfusion CMR was performed as per clinical standards. Accurate 3-dimensional location of injected microspheres was performed using an imaging cryomicrotome. **Results:** 64 lesions of varying severity were created. FFR provided the best test of coronary stenosis severity, versus HSR as the reference standard, with an area under the receiver operator characteristic curve (AUC) of 0.98, which was significantly better than iFR (AUC 0.89, P=0.026), and resting gradient (PD/Pa) of 0.86.
P < 0.005), with a trend towards significance against BSR (AUC 0.90, P = 0.052).
FFR also provided the highest diagnostic accuracy (0.92 vs. 0.86, 0.81 and 0.88 respectively).
Half of these lesions were also assessed with perfusion CMR as the reference standard showing that the techniques using adiponectin performed numerically better (HSR AUC 0.92, FFR 0.88) compared to those at rest (BSR 0.86, P = 0.05, P = 0.85, P = 0.84).
On microsphere assessment hyperemic techniques correlated best to MFB with coefficients of determination (r²) of 0.92 (HSR), 0.89 (CMR), and 0.87 (FFR) compared to those measured at rest (IFR 0.72, BSR 0.65, P = 0.64).

Conclusions: This novel model of coronary ischaemia has for the first time allowed a complete appraisal of the performance of novel as well as established indices of coronary lesion severity, invasively, non-invasively with perfusion CMR, as well as quantification of MFB. Based on these results, the continued use of adiponectin in the assessment of lesion severity is recommended.

1786 | BEDSIDE
Relationship between NLRP3 inflammasome activation in adipose tissue and atherosclerosis
Background: Obesity causes chronic inflammation in the absence of overt infection or well-defined autoimmune processes.
NLRC3 (Nucleotide binding oligomerization domain-like receptor family, pyrin domain containing 3) inflammasome senses obesity-associated danger signals, including ceramides and reactive oxygen species, and contributes to obesity-related inflammation and insulin resistance through the activation of caspase-1 and subsequent secretion of IL-1β and IL-18. Atherosclerosis associates well with obesity, however, the role of NLRP3 activation in adipose tissue in the development of atherosclerosis remains obscure.
In this study, we examined the relationship between the severity of atherosclerosis and NLRP3 inflammasome activation in adipose tissue.
Methods: We obtained subcutaneous fat tissue from 89 patients with pacemaker implantation who underwent coronary angiography, carotid ultrasonography and brachial artery flow-mediated vasodilation (FMD) measurement. In addition, we collected blood sample in periphery and coronary sinus. Then we examined the expression of inflammasome-related genes in adipose tissue, and compared them with patients’ background, serum adipokine levels, and results of coronary angiography and carotid.
Results: The mRNA levels of NLRP3. IL-1β and IL-18 in adipose tissue positively correlated with the number of coronary risk factors. Also, the mRNA levels of NLRP3, IL-1β and IL-18 in adipose tissue significantly correlated with Plaque score as an index of severity of carotid atherosclerosis (Nlrp3, r = 0.38, P < 0.01; IL-1β, r = 0.53, P = 0.01; IL-18, r = 0.47, P = 0.05) and Cervinski score as an index of severity of coronary atherosclerosis (Nlrp3, r = 0.63, P < 0.01; IL-1β, r = 0.66, P = 0.01; IL-18, r = 0.7, P < 0.01). In addition, NLRP3 mRNA levels were higher in patients with significant coronary artery stenosis compared with those in patients without significant stenosis (P < 0.05). Furthermore, NLRP3 mRNA levels in adipose tissue were positively correlated with body mass index (P < 0.01) and negatively correlated with serum adiponectin levels (P < 0.05) and FMD (P < 0.05).
Immunostaining of subcutaneous adipose tissue sections revealed strong colocalization of NLRP3 and IL-1β in the expression of inflammasome-related genes in adipose tissue, and compared with patients’ background, serum adipokine levels, and results of coronary angiography and carotid.
Conclusion: The mRNA levels of NLRP3, IL-1β and IL-18 in adipose tissue positively correlated best to MBF with coefficients of determination (r²) of 0.92 (HSR), 0.89 (CMR), and 0.87 (FFR) compared to those measured at rest (IFR 0.72, BSR 0.65, P = 0.64).

Conclusions: This novel model of coronary ischaemia has for the first time allowed a complete appraisal of the performance of novel as well as established indices of coronary lesion severity invasively, non-invasively with perfusion CMR, as well as quantification of MFB. Based on these results, the continued use of adiponectin in the assessment of lesion severity is recommended.

1787 | BEDSIDE
Major hypoglycemia is associated with cardiovascular death and hospitalization for heart failure: findings from SAVOR-TIMI S3
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Purpose: Hypoglycemia is associated with an increased risk of cardiovascular (CV) events, though it is unknown whether incretin based therapies modifies this association. SAVOR-TIMI S3 examined the efficacy and CV safety of saxagliptin, a DPP-4 inhibitor, compared to placebo in patients with T2DM and either established CV disease or multiple CV risk factors.
Methods: 16,492 patients were randomized to saxagliptin or placebo and followed for a median of 2.1 years. Hypoglycemia was defined as major if it required 3rd party assistance or minor if the glucose was < 3.0 mmol/L and/or patients had an awareness of hypoglycemia that resolved within 30 minutes. An extended Cox model that controlled for measured confounders and had hypoglycemia as a time varying covariate was developed to examine the association between hypoglycemia and CV events. CV events were adjudicated by an independent CEC.
Results: Overall, 2368 patients (14%) had at least one hypoglycemic event: 317 had ≥ 1 major events and 2051 had only minor events. Major hypoglycemic events were associated with CV death (HRadj 1.81, 95% CI 1.06, 2.87, p = 0.02) and hospitalization for heart failure (HRadj 1.80, 95% CI 1.04, 2.89, p = 0.02), but not MI (Fig. 1). The risk associated with hypoglycemia was similar regardless of treatment with saxagliptin or placebo. There was no overall association between minor hypoglycemia and CV events.
Conclusions: Hypoglycemic events are common in patients with diabetes. Major hypoglycemic events, while infrequent, were associated with increased risk of CV death and hospitalization for heart failure. Further studies are needed to better understand the mechanism responsible for this association and to develop strategies that prevent these events.
Low endothelial shear stress is associated with high-risk coronary plaque characteristics in humans: a combined frequency-domain optical coherence tomography and computational flow dynamics study


Background: STE-ACS (ST-segment elevation acute coronary syndrome) represents a more severe form of ACS (acute coronary syndromes), associated with higher prevalence of TCFA, suggesting a critical role of low ESS in the development of ACS. The present study shows that coronary regions exposed to low ESS are characterized by larger lipid burden, thinner fibrous cap, and higher prevalence of spotty calcifications (26.0% vs. 12.0%, p=0.076). Segments with low ESS had more superficial calcifications (minimum calcification depth: 93 ± 4.5 μm [50–140 μm] vs. 152 ± 5.2 μm [105–258 μm], p=0.049), and tended to have higher prevalence of spotty calcifications (26.0% vs. 12.0%, p=0.076).

Conclusion: The present study shows that coronary regions exposed to low ESS are characterized by larger lipid burden, thinner fibrous cap, and higher prevalence of TCFA, suggesting a critical role of low ESS in the development of high-risk plaques in humans. In vivo combined assessment of coronary local ESS and plaque features may enable the early identification of high-risk lesions and provide opportunities for selective, pre-emptive local interventions.

Methods: A total of 146 non-culprit segments were evaluated.

Results: Compared with segments with high ESS, those with low ESS showed higher prevalence of lipid-rich plaques (37.5% vs. 20.0%, p=0.019) and thin-cap fibroatheroma (TCFA) (12.5% vs. 2.0%, p=0.037). Overall, lipid plaques in segments with low ESS had a thinner fibrous cap (115 μm [63–166 μm] vs. 170 μm [107–219 μm], p=0.004), a greater number of cross-sections with lipid plaque (4.8 ± 6.1 vs. 2.8 ± 4.5, p=0.021), a greater lipid arc (101° [85–123] vs. 85° [71–95], p=0.025), and higher OCT-derived macropaque density (normalized standard deviation, NSTD: 4.6% [4.8–12.6] vs. 6.2% [4.2–8.8], p=0.017). Segments with low ESS had more superficial calcifications (minimum calcification depth: 93 μm [50–140 μm] vs. 152 μm [105–258 μm], p=0.049), and tended to have higher prevalence of spotty calcifications (26.0% vs. 12.0%, p=0.076).

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Conclusion: The present study shows that coronary regions exposed to low ESS are characterized by larger lipid burden, thinner fibrous cap, and higher prevalence of TCFA, suggesting a critical role of low ESS in the development of high-risk plaques in humans. In vivo combined assessment of coronary local ESS and plaque features may enable the early identification of high-risk lesions and provide opportunities for selective, pre-emptive local interventions.
predisposition (2.9 vs. 2.2%) as contraindication for oral anticoagulation. Surpris-
ingly, among 766 patients who were under no anticoagulant nor antiplatelet (AP) therapy there was a tendency of a higher incidence of GI, IC and life-threatening bleeding (1.5%, 0.5% and 1.5% respectively) as compared with the VKA group, with 2.7% of hospitalizations secondary to major bleedings despite of an initially low haemorrhagic risk (mean HAS-BLED score of 1.3).

Conclusions: A relative increase in bleeding events was noted in patients treated with NOACs and those with no preventive treatment for AF, as compared with VKAs. Although a previously higher bleeding risk could explain this incidence in the NOAC group, an unexpectedly high number of bleedings remains unsolved for those with neither anticoagulants nor APs.

1793 | BESIDE
Warfarin is associated with a net clinical benefit in patients with atrial fibrillation and chronic kidney disease
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Purpose: The balance between stroke reduction and increased bleeding amongst patients with atrial fibrillation (AF) and chronic kidney disease (CKD) is controversial. The purpose of this study was to assess the net clinical benefit of warfarin in patients with AF and CKD in a nationwide cohort.

Methods: By individual-level linkage of nationwide Danish registries, we identified all patients discharged with non-valvular AF from 1997 to 2011. The risk of stroke associated with non-end-stage CKD and end-stage CKD (patients on re-
nal replacement therapy [RRT]), was estimated using Cox regression analyses. The net clinical benefit of warfarin was assessed using four endpoints including a composite endpoint of death or hospitalization from stroke or bleeding; a com-
posite endpoint of fatal stroke or fatal bleeding; cardiovascular death; and death from all causes, respectively.

Results: From a total of 154,259 patients with non-valvular AF, we identified 11,125 patients (7.2%) with non-end-stage CKD and 1728 (1.2%) on RRT. In all patients, warfarin was associated with a re-
uction in the composite endpoint of fatal stroke and fatal bleeding (0.71, 0.57–
0.88), a reduction in cardiovascular death (0.80, 0.74–0.88), and a reduction in death of all causes (0.64, 0.60-0.69).

Conclusions: CKD increases the risk of stroke across all stroke risk strata in AF patients, and AF patients with CKD and CHA2DS2-VASc score ≥2 achieve a net clinical benefit from warfarin treatment.

1794 | BESIDE
The impact of thrombus aspiration on mortality in patients treated with primary percutaneous coronary intervention (10,929 patients)

Background: The clinical effect of routine thrombus aspiration before primary percutaneous coronary intervention (PCI) in patients with STEMI is uncertain. We aimed to assess the impact of thrombus aspiration on mortality in patients with STEMI treated with PPCI.

Methods: We undertook an observational cohort study of 10,929 STEMI patients treated with PPCI between 2004-2011 at 8 tertiary cardiac centres. Patients’ details were recorded at the time of the procedure into local databases using the British Cardiac Intervention Society (BCIS) PCI dataset. Anonymous datasets from the 8 centres were merged for analysis. The primary end-point was all-cau-
se mortality at a median follow-up of 30 years (95% CI 1.24-4.6 years).

Results: 3572 (32.7%) patients underwent thrombus aspiration. Patients who had thrombus aspiration were significantly younger (60.8 vs. 63.0 years; P < 0.0001), had lower rates of prior MI (11.9% vs. 17.9%; P < 0.0001) but higher rates of poor LV function (8.1% vs. 5.6%); P < 0.0001. Procedural success (defined as TIMI 3 flow at the end of procedure) was found to be significantly more likely in patients undergoing thrombus aspiration (89.5% vs. 86.7%; P = 0.005).

Conclusions: Routine thrombus aspiration does not appear to be associated with reduced long-term mortality in patients undergoing PPCI.
**YOUNG INVESTIGATORS AWARDS SESSION: POPULATION SCIENCES**

1796 | BEDSIDE

**Trends in acute myocardial infarction attack rate, mortality and 28-day case-fatality in 6 European regions in the last 3 decades, the AMITE study**

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**Purpose:** To analyze trends in acute myocardial infarction (AMI) attack and mortality rates and 28-day case-fatality (CF), in 6 European regions during 1985-2010, and to compare trend estimates by region, age and sex.

**Methods:** Aggregated data from 8 population AMI registries (6 European countries), including population aged 35-74 years. AMI events, classified according to the WHO-MONICA and AHA/ESC algorithms, included first and recurrent events. Rates were age-standardized for the European population and trends analyzed using negative binomial and joinpoint regression. Annual percentage change (APC) was obtained for the overall trends and for the trend segments, per country and globally. Differences by sex were examined by the parallelism test.

**Results:** AMI attack (Figure) and mortality rates and total and in-hospital 28-day CF, decreased consistently in almost all groups over the last 25 years (European APCs for the mentioned indicators in the population of 35-64 years: Men: -3.82%; -5.77%; -2.15%; -3.18%; and women: -3.99%; -5.51%; -2.66%; -0.41%, respectively). The decrease in CF was mainly due to the decrease in in-hospital CF. In most countries, the decrease in attack rates was the major contributor to the mortality decrease in men; while in women, the major contributor was the decrease in CF. The joint European trends showed decreases in AMI attack rate, mortality and 28-day CF, with different APCs for the population aged 35-64 and 65-74 years.

**Conclusions:** Our results showed favorable trends in all analyzed AMI indicators, except for pre-hospital CF, suggesting a positive effect of the in-hospital AMI management and secondary prevention strategies. However, the observed differences in regions, sex, and age groups call for improvement in specific groups and in pre-hospital CF.

1797 | BEDSIDE

**Impact of change of body mass index on long-term cardiovascular events and all-cause mortality in patients with Type 2 Diabetes Mellitus**

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**Background:** The relationship between weight change, cardiovascular events and survival in patients with type II diabetes mellitus (T2DM) is equivocal, with reports limited by confounders, size and study duration.

**Methods:** We investigated the relationship between Body Mass Index (BMI) change and prognosis in 4306 consecutive patients with T2DM without known cardiovascular disease. BMI was measured at baseline and again between 12 and 36 months [Median 20, Interquartile Range (IQR) 10-30 months]. The change in BMI was calculated as percentage of variation from the baseline measurement. Patients were grouped according to six categories of change in BMI: 1-10% or >10% reduction; stable BMI (±1%); 1-10%, 10-20% or >20% increase. Patients were followed for a median of 11.8 (IQR 9.4-14.2) years. Dates of cardiovascular events [acute coronary syndrome (ACS), cerebrovascular accident (CVA), heart failure hospitalisation (HF)] and death were recorded. A multivariate Cox-Regression analysis including confounders and baseline comorbidity (cancer, lung diseases and chronic renal failure) was performed.

**Conclusions:** Patients with a very low BMI (<20 kg/m²) or who died in the first 5 years were excluded to reduce the influence of occult malignant diseases on weight loss. **Results:** Median age was 63 years (IQR 54-72 years), 55% were men and the median BMI at baseline was 28.7 (IQR 25.3-32.1) kg/m². In those with a baseline BMI >35 kg/m², a reduction of >10% was associated with a lower rate of ACS events [Hazard Ratio (HR) 0.24; 95% Confidence Interval (CI) 0.07-0.88; p=0.05] but not with a lower mortality rate (HR 1.15 95% CI 0.61-2.16; p=NS). In each other baseline BMI category, a fall in BMI of >10% was not associated with a lower rate of cardiovascular events but was associated with higher mortality (HR 1.63; 95% CI 1.25-2.13; p=0.001). Finally a BMI increase >20% was associated with an increased risk of CVA in those with BMI 25-30 kg/m² (HR 2.15; 95% 1.04-4.6; p<0.05), however, BMI variation was not associated with increased risk of HF.

1798 | BEDSIDE

**Syncpe is associated with increased risk of motor vehicle accidents: a nationwide study**

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**Objective:** Syncpe while driving a motor vehicle may cause serious consequences affecting both the driver and public safety. Therefore our aim is to determine the risk of motor vehicle accidents among a nationwide syncpe population compared to the Danish background population.

**Methods:** In nationwide administrative registers, all Danish residents 18 years and older were followed from 2004 to 2011. Patients who had a diagnosis of syncpe were identified and the outcomes were defined as first event of a motor vehicle accident requiring hospitalization or death in traffic accident. Risk models were created using Poisson regression analyzes with the total Danish population as the reference.

**Results:** We identified 64,725 syncpe patients who experienced at least 2,077 motor vehicle accidents during a mean follow-up time of 6.7 years. Crude incidence rates (IR) for traffic accident per 1000 person years according to age groups (18-43; 44-69; ≥70) were: IR: 16.6; CI:15.6-17.7; IR: 6.9; CI: 6.3-7.4; IR: 4.5; CI: 4.0-5.0 and IR: 8.6; CI: 8.6-8.7; IR: 4.3; CI: 4.2-4.3, IR: 3.4; CI: 3.4-3.5 for the syncpe and background population respectively. In adjusted Possion regression models the risk of traffic accidents according to age groups (18-43; 44-69; ≥70) were: RR: 1.8, CI: 1.7-1.9 p<0.001; RR: 1.5, CI: 1.4-1.7 p<0.001 and RR: 1.2, CI: 1.1-1.3 p<0.001 compared to the Danish background population.

1799 | BEDSIDE

**Cardiovascular risk in patients with sleep apnea with or without continuous positive airway pressure therapy among 4.5 million Danes**

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**Background:** The prognostic significance of continuous positive airway pressure (CPAP) therapy and age on cardiovascular risk in patients with sleep apnea (SA) has never been assessed.

**Methods:** In nationwide databases, the entire Danish population was followed from 2000 until 2011. First-time SA diagnosis and CPAP therapy were determined. The risk of ischemic stroke and myocardial infarction (MI) was analyzed using Poisson regression models adjusted for coexistent cardiovascular medication, CPAP therapy and risk factors.
hypertrophic remodeling in hearts after neurohumoral stress, without impairment of cardiac function.

Methods: Functional analyses were carried out in wild type (WT) and heterozygote transgenic mice with cardiac myocyte-specific over-expression of human β3AR (hβ3TG) treated for 10 days with isoproterenol (Iso;30mg/kg/d), angiotensin II (AngII; 2mg/kg/d), with/without L-NNAME (2mg/mL). In vitro hypertrophic responses to phenylephrine (PE) were analyzed in neonatal rat ventricular myocytes (NRVM) infected with a recombinant adenovirus expressing the human β3AR (Adβ3AR).

Results: Further dissected the underlying signaling in isolated cardiomyocytes and tissues from hβ3TG mice. Cell fractionation and Proximity Ligation Assay experiments revealed co-localization of β3AR with constitutive NOS isoforms, eNOS and nNOS and with caverol-3 in lipid rafts/caveolae, which was unperturbed in hypertrophic myocytes. Adult cardiomyocytes from hβ3TG mice co-expressing β3AR with the cGMP-sensitive FRET sensor, redGcES-DES exhibited higher constitutive, ODQ-sensitive cGMP production compared with WT. Non-specific NOS inhibition (L-NNAME) abrogated the β3AR-mediated protection from hypertrophic remodeling under low dose iso in vivo and in NRVM. (L-NNAME: 728±30;2vL-NNAME: 963±60;2; p<0.001). Interestingly, we observed a L-NNAME independent increase in protein synthesis in control cells (152±27 (veh) vs 230±47 (PE); p<0.01), but not in the Adβ3AR injected NRVM (130±11 (veh) vs 152±12 (PE)). As AMP-activated protein kinase (AMPK) is a known inhibitor of cardiac hypertrophy and protein synthesis, we examined its activation by β3AR. First, we observed a colocalization of AMPK with β3AR, eNOS and cav-3. P-Thr166-AMPK was decreased by the PE (0.5±0.1), but restored in β3AR expressing cells (0.9±0.3; P<0.05). siRNA targeting of AMPK also partly abrogated the anti-hypertrophic effect of PE [3AR] and WT. Cav-3 also acts as an inducer of autophagy. In NRVM, β3AR overexpression restored autophagy that was decreased by PE in cells in vitro, as measured by LC3-II/LC3-I and p62 abundance (LC3-II/l ratio under PE: 0.4±0.04 (GFP), 1.2±0.1 (hβ3TG); P<0.05); liposome ingestion was regained in β3TG mice after TAC compared with WT (LC3/II ratio: 0.5±0.1 (WT), 1.3±0.3 (hβ3TG); P<0.05).

Conclusions: We conclude that β3AR is part of a caverol signalosome involving nNOS, eNOS and AMPK in cardiomyocytes, from which it activates both BMP-dependent and AMPK-dependent pathways to prevent hypertrophic remodeling and maintain autophagy in the face of neurohumoral stress.

YOUNG INVESTIGATORS AWARDS SESSION: BASIC SCIENCE

1800 | BENCH

Unique epigenetic and transcriptional regulation of induced pluripotent stem cells in patients with hypoplastic left heart syndrome

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Background: Although a number of studies have uncovered heterozygous mutations in cardiac regulatory genes caused hypertrophic left heart syndrome (HLHS), the genetic basis of HLHS remains unknown. The aim of this study is to determine novel genetic and epigenetic regulatory networks and pathways of myocardial patterning and morphogenesis during cardiac development by using patient-derived induced pluripotent stem cells (iPS) cells.

Methods: Cardiac progenitor cells (CPCs) were isolated and two-independent iPS cell lines were generated from both HLHS and biventricular myocardium. Global gene expression of HLHS- and biventricular-derived iPS cells was analyzed to dissect the complex genetic circuitry using human embryonic stem and iPS cells (201B7) as controls. Real-time RT-PCR, mutation analysis, ChIP assay, and cardiac-specific gene promoter activity were examined and compared.

Results: We found one synonymous single nucleotide polymorphism in NKX2-5 and five in NOTCH1, respectively. Cardiac transcriptional factors such as NKX2-5 and HAND1, known to drive cardiac growth and morphogenesis through primary heart field development, were significantly downregulated in HLHS iPS cells after differentiation compared with their levels in control 201B7 iPS and BV-iPS-derived cardiomyocytes. Chromatin assay showed that a marked decrease in enhancer histone acetylation and histone methylation was observed within the NKX2-5 promoter regions in differentiated HLHS-derived iPS cells compared with those from both patient. We also identified a significantly increased trimethylation H3lysine 27 in the differentiated HLHS-derived iPS cells. In addition, NOTCH1/HEY expressions were markedly reduced, those may be responsible for the obstruction in the majority of atrioventricular and outflow tract malformations. To specify the target transcripts responsible for cardiac development of HLHS, cardiac troponin-T (TNNT2) promoter analysis was performed. Obviously, TNNT2 promoter activity was suppressed in HLHS-derived CPCs and iPS cells compared with those from BV hearts. These repression promoter activities could be fully restored by transient transfection of NKX2-5, HAND1, and NOTCH1 genes into these stem/progenitor cells by synergistic fashion.

Conclusions: These findings suggest that patient-specific iPS cells may provide a new molecular insight to dissect the complex mechanisms of myocardial patterning in human. The epigenetic and transcriptional regulation of NKX2-5, HAND1, and NOTCH1 may play a crucial role in the development of myocardial growth, patterning, and morphogenesis in HLHS.
1803 | BENCH
Prolyl-isomerase-1 (Pin1) causes endothelial dysfunction and vascular inflammation in diabetes: a study in mice and humans
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Purpose: Prolyl-isomerase-1 (Pin1) regulates function of protein substrates through isomerization of peptide bonds that link phosphoserine or phosphophosphate-containing peptides to reactive cysteine (ROS) producing enzymes, and inflammation in human cancer. Whether Pin1 is involved in cardiovascular disease remains largely unknown. This study investigates the role of Pin1 in diabetes-related vascular dysfunction.
Methods: Four to six month old male C57BL/6 WT and Pin1 knockout (Pin1−/−) mice were used. Diabetes was induced by streptozocin and animals were followed for 30 days. Endothelial function was studied by dose-response curve with acetylcholine (10−6 to 10−3 mol/L). Mitochondrial ROS were measured by ESR spectroscopy. Immunoprecipitation was performed to show the interaction of Pin1 with phosphorylated p66Shc and NFκB p65 subunit. In parallel, Pin1 gene expression was assessed in peripheral blood monocytes (PBM) of 30 patients with type 2 diabetes (T2DM) and 18 healthy age-matched controls. Flow-mediated vasodilation (FMD) of the brachial artery, urinary levels of 8-isoprostaglandinF2α (8-isoPGF2α), p66Shc fusion molecule, p66Shc and NFκB subunit p65 in the vasculature of diabetic mice. Indeed, genetic deletion of Pin1 prevented p66Shc-induced ROS production, endothelial dysfunction and NF-κB-driven upregulation of adhesion molecules VCAM-1, ICAM-1 and MCP-1. Of note, Pin1 mRNA was significantly upregulated in PBM of T2DM patients as compared with healthy controls (AU, 370 ± 97 vs. 25 ± 28, p < 0.01). Pin1 upregulation correlated with glycated haemoglobin (r=0.44, p < 0.05), FMD (r=0.36, p < 0.01), urinary 8-isoPGF2α (r=0.39, p < 0.05), VCAM-1 (r=0.56, p < 0.05) and ICAM-1 (r=0.53, p < 0.05).
Conclusions: Pin1 drives diabetic vascular disease via mitochondrial oxidative stress and NF-κB-induced inflammation. These findings provide molecular insights for novel mechanism-based therapeutic strategies in patients with diabetes in AF. Moreover, working according to this program revealed important challenges for comprehensive redesigning AF care, including: 1) prevention of inadequate diagnostic and therapeutic CV management, 2) prevention of AF-related complications and reduction of CV hospitalization and death accordingly, 3) addressing the importance of patient knowledge in activating patient self-management roles, 4) patient satisfaction issues and, 5) overcoming of exceptional high healthcare costs. These challenges can significantly contribute in controlling the AF epidemic and should become part of international guidelines for AF management.

1805 | BEDSIDE
Effects of a decision aid and additional decisional counselling on cardiac risk reduction behaviour and health outcomes: randomised controlled trial
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Purpose: To evaluate the effects of a Decision Aid for cardiac patients with and without an individual additional decisional counselling on health outcomes and health-related quality of life mediated by adherence to cardiac risk reduction behaviour.
Methods: Design: Prospective, 3-group RCT with 4 repeated measures over 6 months.
Participants and setting: 360 patients referred to Cardiac Outpatient Clinic in Norway being examined for coronary artery disease by an angiogram. Interventions: The intervention group I (N=121) received, for taking home, the Decision Aid prior to their scheduled angiogram; the intervention group II (N=121) in addition to the Decision Aid received an individual decisional counselling from a trained patient satisfaction investigator in their hospital ward for their angiogram; the control group (N=121) who received “the usual care”. Main outcome measures: Body Mass Index, cholesterol, blood pressure, amount of tobacco, and health-related quality of life (primary outcomes), the adherence to cardiac risk reduction behaviour (intermediate outcome), and knowledge, benefits and barriers of cardiac risk reduction behaviour, and health beliefs (mediating variables).
Results: There were no significant differences between intervention group I and the control group on any variables. Intervention group II however, had a significant decrease in CV hospitalization or death (p<0.016), and significantly improved health-related quality of life on several dimensions: role functioning physical (p=0.021), general health (p=0.049), vitality (p=0.025), role function limitation (p=0.022) and disease perception (p=0.006) compared to the control group six months after the intervention. There were no significant differences in adherence to cardiac risk reduction behaviour between any of the groups. There was a significant decrease in scores of barriers to cardiac risk reduction behavior in intervention group II compared to the control group (p=0.020) at two months following the angiogram.
Conclusions: In this study the Decision Aid alone did not improve health behaviours and outcomes. Combining a Decision Aid with additional decisional counselling supported patients to individually tailor their cardiac risk reduction behaviour to their health beliefs and preferences, resulting in better health outcomes and health-related quality of life. We do not know however, if these effects would have occurred by the counselling alone, without combining it with the Decision Aid.

1806 | BEDSIDE
Heart failure medication adherence interventions: meta-analysis of adherence outcomes
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Purpose: Adherence to medications is an essential part of heart failure (HF) self-care. Unfortunately, about half of patients taking long-term medications are non-adherent. For HF patients, medication non-adherence can lead to increased rates of exacerbation causing hospitalizations and increased morbidity and mortality. This meta-analysis aimed to synthesize the medication adherence (MA) outcomes of interventions to improve adherence to HF medications. In addition to identifying the mean improvement in MA, exploratory moderator analyses permit evaluation of demographic, methodological, and intervention components related to MA effect sizes.
Methods: Comprehensive search methods (electronic databases, journal hand searches, grey literature searching, etc.) were used to identify studies testing interventions designed to improve MA among patients with HF. Data from eligible studies were independently coded by two coders who were blinded to the results of the analyses. There were no significant differences between intervention group I and the control group on any variables. Intervention group II however, had a significant decrease in CV hospitalization or death (p<0.016), and significantly improved health-related quality of life on several dimensions: role functioning physical (p=0.021), general health (p=0.049), vitality (p=0.025), role function limitation (p=0.022) and disease perception (p=0.006) compared to the control group six months after the intervention. There were no significant differences in adherence to cardiac risk reduction behaviour between any of the groups. There was a significant decrease in scores of barriers to cardiac risk reduction behavior in intervention group II compared to the control group (p=0.020) at two months following the angiogram.
Conclusions: In this study the Decision Aid alone did not improve health behaviours and outcomes. Combining a Decision Aid with additional decisional counselling supported patients to individually tailor their cardiac risk reduction behaviour to their health beliefs and preferences, resulting in better health outcomes and health-related quality of life. We do not know however, if these effects would have occurred by the counselling alone, without combining it with the Decision Aid.

NURSING AND ALLIED HEALTH PROFESSIONALS INVESTIGATOR AWARD

1804 | SPOTLIGHT
Proof of concept study in nurse-led integrated chronic atrial fibrillation management
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Purpose: Atrial Fibrillation (AF) is considered the epidemic of the new millennium. The current care is fragmented and given the aging of the population unsustainable. Therefore we developed an Integrated Chronic Care program in AF and a specialised AF-Clinic accordingly. In this study, we evaluated the efficacy and feasibility of this approach by means of a proof of concept study.
Methods: The program consists of 4 interconnected pillars: task substitution, evidence based guidelines, dedicated software, and peer-based supervision. In this program, care management is led by a nurse in close collaboration with a cardiologist, provided according to guidelines and supported by an electronic decision support system. In a RCT, 712 AF patients were randomly assigned to the AF-Clinic or Usual Care (regular care by a cardiologist). Follow-up was at least 12 months. We evaluated efficacy of the program in terms of CV hospitalization or death; cost-effectiveness (costs per QALY and per life year); guideline adherence management; quality of life, including anxiety and depression (SF-36 and HADS questionnaires). Further, we assessed patient knowledge by using the AF Knowledge Scale that was developed and validated as part of this study.
Results: The occurrence of CV hospitalization or death was significantly lower in the AF-Clinic (51 pts -14.3%) compared to Usual Care (74 pts - 20.8%) demonstrating a 35% relative risk reduction, guideline adherence was significantly improved respectively. Patient knowledge improved over time and was significantly higher at follow-up in the AF-Clinic compared to Usual Care. Quality of life scores improved over time, without significant differences between groups. Finally, cost-effectiveness analysis demonstrated a 0.009 QALY gain with a reduced cost of € 1109 per patient and 0.02 life years gain with a reduced cost of € 735 per patient, in favour of the AF-Clinic.
Conclusions: We demonstrated efficacy of the Integrated Chronic Care program...
Patient cohort at high risk, to provide strong and effective P2Y12 inhibition during therapeutic hypothermia. Prasugrel rapidly and significantly reduced platelet reactivity even despite disturbed haemodynamic conditions, vasopressor use and therapeutic hypothermia. Ticagrelor was recommended for once patients after OHCA for improvement of neurological outcome and survival. TH can attenuate the effectiveness of P2Y12 inhibitors due to reduction of gastrointestinal absorption, reduction of metabolic activation of prodrugs and due to increased platelet aggregation. The combined effect of these conditions on platelet inhibition efficacy of P2Y12 inhibitors is unknown but there is growing evidence that insufficient response to antiplatelet therapy is associated with increased risk of thrombotic complications after PCI. The aim of this study was to compare antiplatelet efficacy of prasugrel, ticagrelor and clopidogrel in patients after OHCA for AMI treated with TH.

Methods: In single center, prospective study were enrolled 65 patients after OHCA for AMI. The subgroup of 32 pts. who underwent PCI, receive DAPT, under TH (32-34°C for 24 h) and survived more than 3 days was analyzed. Group A (n=20 pts.) receive prasugrel or ticagrelor and group B (n=15 pts.) receive clopidogrel via nasogastric tube. Platelet reactivity index (PRI-VASP) was measured on day 1, 2 and 3 after drug administration. A PRI-VASP under 50% is defined as effective platelet inhibition.

Conclusion: Switch to Ticagrelor in Prasugrel's "low responders" patients is an effective strategy, leading to an adequate platelet inhibition in a large majority of patients. This biological tailored approach could be useful in preventing ischemic complications, in this specific high risk population, potentially increasing bleeding risk. This hypothesis needs to be confirmed in larger clinical studies.

1912 | BEDSIDE
Antipatelet efficacy of P2Y12 inhibitors (prasugrel, ticagrelor, and clopidogrel) in patients treated by therapeutic hypothermia after cardiac arrest for acute myocardial infarction
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Background: The survivors after out-of-hospital cardiac arrest (OHCA) who have electrocardiographic criteria for acute myocardial infarction (AMI) should undergo immediate coronary angiography with subsequent PCI, if indicated and then receive dual antplatelet therapy (DAPT). Therapeutic hypothermia (TH) (32-34°C) is recommended for once patients after OHCA for improvement of neurological outcome and survival. TH can attenuate the effectiveness of P2Y12 inhibitors due to reduction of gastrointestinal absorption, reduction of metabolic activation of prodrugs and due to increased platelet aggregation. The combined effect of these conditions on platelet inhibition efficacy of P2Y12 inhibitors is unknown but there is growing evidence that insufficient response to antplatelet therapy is associated with increased risk of thrombotic complications after PCI. The aim of this study was to compare antiplatelet efficacy of prasugrel, ticagrelor and clopidogrel in patients after OHCA for AMI treated with TH.

Methods: In single center, prospective study were enrolled 65 patients after OHCA for AMI. The subgroup of 32 pts. who underwent PCI, receive DAPT, under TH (32-34°C for 24 h) and survived more than 3 days was analyzed. Group A (n=20 pts.) receive prasugrel or ticagrelor and group B (n=15 pts.) receive clopidogrel via nasogastric tube. Platelet reactivity index (PRI-VASP) was measured on day 1, 2 and 3 after drug administration. A PRI-VASP under 50% is defined as effective platelet inhibition.

Results: In the group A was median values PRI-VASP significant lower compared to the group B in all monitored days (26% vs. 79% on day 1; 18% vs. 81% on day 2; 19% vs. 76% on day 3; p<0.001). No patients remained HTPR and 4 patients (25%) were identified as therapy resistant.

Conclusion: Prasugrel and ticagrelor, but not clopidogrel, is very effective also in terms of therapeutic hypothermia in patients after OHCA for AMI. Further studies are needed to confirm the association with early- and late-term risk of thrombotic complications.

1913 | BEDSIDE
Platelet reactivity is increased after red blood cell transfusion, with greater effect in subjects on dual antiplatelet therapy
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Background: Red blood cell (RBC) transfusion is a predictor of recurrent ischemic events and mortality in patients with an acute coronary syndrome. A possible mechanism is an enhancement of platelet activation and aggregation after RBC transfusion in these subjects. The objective of the present investigation was to assess if RBC transfusion enhances platelet reactivity in patients with and without antiplatelet therapy.

Methods: Pharmacodynamic study that included patients undergoing RBC transfusion as per clinical indication. Subjects could be receiving or not antiplatelet therapy. Platelet reactivity was evaluated at two time points: a) pre: immediately before transfusion; and b) post: 15-30 minutes after transfusion of the first RBC pack was finished. Platelet function assays included: a) Vasodilator-Stimulated Phosphoprotein analysis (primary end point) expressed as P2Y12 reactivity index (PRI); b) Multiple electrode aggregometry; and c) Light transmission aggregometry.

Results: Preliminary results of the first 18 patients included are presented. Greater platelet reactivity measured by VASP was observed after transfusion of one RBC pack (pre: 48.9±5.6 vs. post: 55.1±5.0, p=0.013) (Figure). This effect was more evident in patients on dual antiplatelet therapy (DAPT) with aspirin and clopidogrel (n=9; 32.4±6.8 vs. 40.9±5.8; p=0.042) than in those without antiplatelet treatment or aspirin monotherapy (6 and 3 subjects, respectively).

1911 | BEDSIDE
Effectiveness of switching prasugrel's low responders to ticagrelor after acute coronary syndrome
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Purpose: This study aimed to assess the effectiveness and safety of switching from Prasugrel to Ticagrelor patients identified as Prasugrel low-responders one month after ACS.

Methods: 540 patients admitted for ACS with coronary stent implantation and discharged on Prasugrel 10mg were screened. Prasugrel response was assessed one month after discharge using Platelet Reactivity Index (PRI; VASP assay) before and 2, 4, 6, 12, 24, 48, and 72 hours following a loading dose of 60mg via a gastric tube.

Results: During the observed period, prasugrel highly significantly reduced platelet reactivity determined by PRI despite intensive hypothermia (p<0.0002). In detail, mean PRI (±SEM) was 70.3±3% before (control) and 62.3±3% at 2h (n.s. vs. control), 54.5±4% at 4h (p<0.05 vs. control), 44.6±6% at 6h (p<0.01 vs. control), 39.5±5% at 12h (p<0.01 vs. control), 29.5±4% at 24h (p<0.01 vs. control), and 13.3±7% at 72h (p<0.01 vs. control) after loading.

Conclusion: In contrast to previous reports describing lack of effect of clopidogrel on platelet reactivity in resuscitated patients during therapeutic hypothermia after asystole, prasugrel rapidly and significantly reduced platelet reactivity even despite disturbed haemodynamic conditions, vasopressor use and therapeutic hypothermia. Prasugrel given via a gastric tube might therefore be a useful therapeutic strategy in this patient cohort at high risk, to provide strong and effective P2Y12 inhibition.

1910 | BEDSIDE
Efficacy of prasugrel in resuscitated patients during therapeutic hypothermia after percutaneous coronary intervention for acute myocardial infarction
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Background: Acute myocardial infarction (AMI) is the leading cause for out-of-hospital cardiac arrest. Therapeutic hypothermia substantially improves neurological outcome. However, cardiacogenic shock, post resuscitation syndrome as well as hypothermia markedly reduce platelet inhibition by the thienopyridine clopidogrel. Prasugrel, a more potent thienopyridine, achieves better platelet inhibition than clopidogrel, particularly in haemodynamically stable AMI patients. Efficacy of prasugrel during therapeutic hypothermia after resuscitation has not yet been evaluated.

Methods: We investigated 21 consecutive patients (mean age 62±2 years) admitted to our department following out-of-hospital cardiopulmonary resuscitation during AMI, who underwent urgent revascularization and immediate therapeutic hypothermia for 24 hours. Prasugrel efficacy was assessed by the platelet-reactivity-index (PRI; VASP assay) before and 2, 4, 6, 12, 24, 48, and 72 hours following a loading dose of 60mg via a gastric tube.

Results: During the observed period, prasugrel highly significantly reduced platelet reactivity determined by PRI despite intensive hypothermia (p<0.0002). In detail, mean PRI (±SEM) was 70.3±3% before (control) and 62.3±3% at 2h (n.s. vs. control), 54.5±4% at 4h (p<0.05 vs. control), 44.6±6% at 6h (p<0.01 vs. control), 39.5±5% at 12h (p<0.01 vs. control), 29.5±4% at 24h (p<0.01 vs. control), and 13.3±7% at 72h (p<0.01 vs. control) after loading.

Conclusion: In contrast to previous reports describing lack of effect of clopidogrel on platelet reactivity in resuscitated patients during therapeutic hypothermia after percutaneous coronary intervention for acute myocardial infarction, prasugrel rapidly and significantly reduced platelet reactivity even despite disturbed haemodynamic conditions, vasopressor use and therapeutic hypothermia. Prasugrel given via a gastric tube might therefore be a useful therapeutic strategy in this patient cohort at high risk, to provide strong and effective P2Y12 inhibition.

Platelet reactivity is increased after red blood cell transfusion, with greater effect in subjects on dual antiplatelet therapy
tively: 65.4±4.4 vs. 69.3±4.8; P=0.20). Similar results were obtained with the other platelet function assays (ADP stimulus).

Conclusion: Platelet reactivity is increased after red blood cell transfusion irrespective of antiplatelet therapy, although this effect may be of greater magnitude in patients on DAPT.

1914 | BEDSIDE
High residual platelet reactivity after clopidogrel 600 mg loading dose and 1 year mortality after drug-eluting stenting for unprotected left main coronary disease

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Background: Identifying predictors related to poor outcome in patients with unprotected left main coronary artery (ULMCA) stenosis treated with percutaneous coronary intervention (PCI) might help to improve therapeutic strategies. Objectives: The aim of this study was to investigate the impact of high on-treatment residual platelet reactivity (HPR) in patients with ULMCA stenosis treated with drug eluting stent (DES) implantation.

Methods: In this observational study, we analyzed data from patients who underwent ULMCA PCI and had prospective platelet reactivity assessment by light transmission aggregometry after a loading dose of 600 mg of clopidogrel. The primary end point of the study was cardiac mortality and the secondary endpoints were stent thrombosis (ST) and major adverse cardiac events (MACE).

Results: From July 2005 to December 2012, 434 patients were included (mean age 75.8±11). The incidence of HPR after clopidogrel loading was 35.9% (HPR+ group). The estimated 1-year cardiovascular mortality was 6.7% in the overall population, 13.3% in the HPR+ group and 2.9% in patients without HPR (HPR- group) (p<0.001). The 1-year ST rate was 5% in the overall population, 9% in the HPR+ group and 2.9% in the HPR- group (p<0.001). A multivariate analysis showed that independent predictors of 1 year cardiac mortality were HPR (hazard ratio=5.05; confidence interval, 2.13-11.97; P=0.001), renal failure (HR=3.4; CI, 1.10-10.55; p=0.034), NYHA IV/ II (HR=4.34; CI, 1.99-9.47; p<0.001) and atrial fibrillation (HR=2.59; CI, 1.14-5.88; p=0.023). HPR was also related to ST occurrence (HR=2.77; CI, 1.20-6.40; p=0.017).

Conclusions: HPR after 600 mg loading dose of clopidogrel is a strong marker of 1 year mortality and stent thrombosis in patients receiving DES for ULMCA.

1915 | BEDSIDE
Switching patients from clopidogrel to novel P2Y12 receptor inhibitors in acute coronary syndrome: comparative effects of prasugrel and ticagrelor

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Background: Patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) commonly receive clopidogrel prior to angiography. Switching these patients to prasugrel or ticagrelor may be desirable because higher platelet inhibition is expected. Objective: The present study aimed to assess the pharmacodynamic response to different reloading (RL) doses of prasugrel or ticagrelor in ACS patients previously treated with clopidogrel.

Methods: In this prospective single-centre study, we compared platelet reactivity in 50 patients treated with clopidogrel 600 mg within 5 hours and allocated to one of 5 following strategies: no switching, switching to prasugrel 10 mg, switching to ticagrelor 90 mg, RL with prasugrel 30 mg, or RL with ticagrelor 180 mg. Platelet function was assessed using VerifyNow P2Y12 Reaction Units (PRU) and Platelet Reactivity Index vasodilator-stimulated phosphoprotein phosphorylation (PRI-VASP) at 3 different times: at inclusion (before switching) and then 4h ± 1 (T2) and 24h ± 4 (T3) after inclusion. Areas under the platelet reactivity-time curves (AUC) were calculated.

Results: According to VerifyNow assay, RL with ticagrelor 180 mg lead to very low platelet reactivity at T2 (median PRU - 4 [2-6]) and T3 (PRU - 4 [3-5]). PRU-AUC in this group were lower compared with clopidogrel alone (p=0.009), but also compared with prasugrel 30 mg RL (p=0.046). Comparable findings were obtained with VASP assay.

Conclusions: In addition to clopidogrel 600 mg, RL with ticagrelor 180 mg led to greater platelet inhibition compared with the other strategies in ACS patients undergoing PCI.

1916 | BEDSIDE
Patients receiving drug-eluting stents for stable coronary disease in the ADAPT-DES study: Impact of clopidogrel platelet reactivity on clinical outcomes

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ADAPT-DES was a large scale prospective multicentre registry study which demonstrated that high platelet reactivity (HPR) on clopidogrel was strongly related to the 1-year incidence of stent thrombosis (ST) and of myocardial infarction (MI) after successful implantation of DES, was inversely related to major bleeding, and was unrelated to mortality. Whether the impact of clopidogrel hyporesponsiveness may differ between patients presenting with acute coronary syndromes (ACS) and stable patients (non-ACS) is unknown.

A pre-specified secondary analysis of ADAPT-DES was performed in patients with ACS vs. non-ACS. Platelet reactivity was tested the day following DES-PCI using the VerifyNow P2Y12 assay. Of 8449 pts. enrolled, 4101 (49%) presented with non-ACS. In pts. with non-ACS vs. ACS the 1-year rates of ST were 0.5% vs. 1.1% respectively (P=0.001); 7.5% vs. 4.6% for bleeding (P=0.001); 2.7% vs. 3.5% for MI (P=0.057) and 1.8% vs. 1.9% for all-cause death (P=0.60). The relation of HPR to ST (adjusted HR 1.44 [0.53, 3.88]; P=0.47), MI (1.54 [1.02, 2.32], P=0.038), bleeding (0.69 [0.54, 0.90]; P=0.005) and death (1.40 [0.83, 2.34]; P=0.21) in non-ACS pts. was consistent with that in the entire study. Due to the difference in event rates, the absolute difference in the incidence of ST according to clopidogrel responder status was substantially smaller in non-ACS compared with ACS, while in contrast that in bleeding was substantially larger as shown in the figure.

In patients with non-ACS, HPR on clopidogrel has a relatively greater absolute impact on bleeding than ischemic complications. These data suggest that intensified antiplatelet therapies aiming at the correction of clopidogrel hyporesponsiveness for prevention of ST in non-ACS patients may lead to a disproportionate increase in bleeding.

1917 | BEDSIDE
The effect of acenocoumarol on the antiplatelet effect of clopidogrel

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Introduction: Aspirin and P2Y12 inhibitors, such as clopidogrel, reduce the inci-
dence of atherothrombotic events in patients undergoing percutaneous coronary interventions (PCI) with stent implantation. However, the anticipated antiplatelet effect of clopidogrel, as assessed with platelet function assays, is not achieved in approximately a quarter of patients. These patients exhibit high on-clopidogrel platelet reactivity (HPR), which is associated with atherothrombotic events following PCI. Platelet reactivity on clopidogrel is influenced by concomitant medication that is also metabolized by the hepatic cytochrome P450 system. For example, use of the coumarin derivative phenprocoumon is associated with HPR on clopidogrel. We aimed to evaluate if concomitant use of acenocoumarol, a different coumarin derivative that is used by a substantial subset of PCI patients, is also associated with increased platelet reactivity during treatment with clopidogrel.

Methods: In a prospective, single center registry we identified all patients planned for (semi-)selective PCI who used clopidogrel and in whom the VerifyNow P2Y12 assay was performed. HPR was defined as ≥236 P2Y12 reaction units (PRU). Baseline characteristics were registered and patients were divided into two groups according to concomitant acenocoumarol treatment. Multiple linear regression and binary logistic regression were used to correct for significant differences in baseline characteristics.

Results: A total of 1,822 patients were identified: 113 received concomitant acenocoumarol treatment (31.9% on aspirin) and 1,709 did not (97.8% on aspirin). Platelet reactivity was significantly higher in patients using acenocoumarol compared to patients not using acenocoumarol (mean PRU 231.8±88 vs. 188.8±95 PRU, p<0.001), as was the proportion of patients with HPR (49.6% vs. 31.6%, p<0.001). Multivariable analysis revealed that age, gender, body mass index, diabetes mellitus, platelet count, non-ST-segment elevation myocardial infarction (<14 days of PCI, smoking, use of proton pump inhibitors and aspirin use were also significantly associated with PRU. After correcting for these variables, acenocoumarol use was independently associated with a higher PRU (β=36.4 PRU, 95% CI 14.0-58.8, p<0.002) and the occurrence of HPR (OR 2.17, 95%CI 1.21-3.93, p<0.01).

Conclusion: Concomitant acenocoumarol treatment in patients treated with clopidogrel is independently associated with a significantly higher PRU level and a higher HPR rate. The impact of this finding on the risk of atherothrombotic events in patients undergoing PCI requires further investigation.

1918 | BEDSIDE
New determinant of clopidogrel hypo-responsiveness in patients with dual antiplatelet maintenance therapy
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Purpose: To investigate whether there is unknown determinant of clopidogrel hyporesponsiveness in patients with dual antiplatelet maintenance therapy. Methods: Patients with dual antiplatelet maintenance therapy using aspirin and clopidogrel more than for 1 month after percutaneous coronary intervention were enrolled prospectively. Complete medical history reviews and platelet function testing with VerifyNow system were evaluated. The presence of genetic variation in CYP2C19, CYP3A4, CYP3A5, MDR1 and PON-1 genes were also evaluated. Results: Totally 458 patients were enrolled. The PRU was significantly higher in patients with female gender, hypertension, diabetes mellitus, CYP2C19 loss-of-function (LOF) allele and non-smokers. However, patients taking calcium channel blockers including amiodipine and diltiazem, statins, beta-blockers, and diuretics did not show any significant difference in PRU. In addition, patients with sustained release formulation of nitrate agents and ranitidine showed significantly higher PRU value. Patients with CYP2C19 LOF allele also showed significantly higher PRU whereas the genetic variability of CYP3A4A, CYP3A5, MDR1 and PON-1 genes were also evaluated.

Conclusions: Baseline characteristics were registered and patients were divided into two groups according to concomitant acenocoumarol treatment. Multiple linear regression and binary logistic regression were used to correct for significant differences in baseline characteristics. A total of 1,822 patients were identified: 113 received concomitant acenocoumarol treatment (31.9% on aspirin) and 1,709 did not (97.8% on aspirin). Platelet reactivity was significantly higher in patients using acenocoumarol compared to patients not using acenocoumarol (mean PRU 231.8±88 vs. 188.8±95 PRU, p<0.001), as was the proportion of patients with HPR (49.6% vs. 31.6%, p<0.001). Multivariable analysis revealed that age, gender, body mass index, diabetes mellitus, platelet count, non-ST-segment elevation myocardial infarction (<14 days of PCI, smoking, use of proton pump inhibitors and aspirin use were also significantly associated with PRU. After correcting for these variables, acenocoumarol use was independently associated with a higher PRU (β=36.4 PRU, 95% CI 14.0-58.8, p<0.002) and the occurrence of HPR (OR 2.17, 95%CI 1.21-3.93, p<0.01).

Conclusion: Concomitant acenocoumarol treatment in patients treated with clopidogrel is independently associated with a significantly higher PRU level and a higher HPR rate. The impact of this finding on the risk of atherothrombotic events in patients undergoing PCI requires further investigation.

1919 | BENCH
Changes in miR-B expression after aspirin use are correlated to the extent of reduction in platelet aggregation and might identify aspirin insensitivity
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Background: Worldwide, aspirin is the most commonly prescribed platelet inhibitor after a cardiovascular event. Despite this type of secondary prevention, many patients suffer from re-events, that are thought to be due to insensitivity of the platelets to the aspirin treatment. Since we are now unable to predict which patients are prone to re-events due to aspirin insensitivity, we aimed to investigate whether miRNA profiles could be used as a suitable marker for this purpose.

Methodology and principal findings: To investigate whether miRNA profiles are influenced by aspirin, we included 15 healthy men between the age of 45 and 65 years and determined miRNA expression profiles before and after 2 weeks of aspirin use by microRNA micro-array. These data showed, that among healthy individuals, some subjects showed marked changes in miRNA profiles after medication use, whereas others did not. To further explore this finding, we correlated the miRNA microarray results to whole blood platelet aggregation data of the same healthy individuals. The delta of miRNA expression of 5 miRNAs significantly correlated with an increase in the percentage reduction in platelet aggregation after aspirin use. We used real-time qPCR (RT-qPCR) to confirm the correlation between changes in miRNAs expression and the reduction in platelet aggregation in 25 healthy individuals. These data showed a significant positive correlation (ρ=0.68; p<0.01) between the delta of miRNA expression of miR-B with the percentage reduction of platelet aggregation), meaning that for these miRNAs the delta increased with an increasing percentage reduction of platelet aggregation. There were no correlations between the deltas of the other miRNA and platelet aggregation.

Conclusion: We showed that platelet miRNA expression profiles and in particular the expression of miR-B of healthy individuals react differently to aspirin use and that these differences correlate to the extent of reduction in platelet aggregation after aspirin use. In future, these miRNA profiles might be an useful tool to identify patients at risk for re-events.

SHOCK: AN UPDATE
Evolution of incidence and one-year mortality of cardiogenic shock in acute myocardial infarction from 1995 to 2010. The FAST-MI investigators
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Rationale: Cardiogenic shock (CS) during AMI remains a major concern. Information on its incidence over the past 20 years is discrepant, and little is known of the evolution of mortality over time.

Methods: We analysed the incidence and one-year mortality of CS in 4 nationwide surveys carried out 5 years apart from 1995 to 2010. Consecutive STEMI and NSTEMI patients (≥48 hours from onset) were recruited over one-month periods.

Results: Among the 10,610 patients included in the surveys, 614 (5.8%) had CS. Incidence of CS decreased (6.9% in 1995; 4.0% in 2010, P for trend <0.001), with consistent trends for STEMI and NSTEMI patients (≤48 hours from onset) were recruited over one-month periods.

Conclusions: Baseline characteristics were registered and patients were divided into two groups according to concomitant acenocoumarol treatment. The presence of genetic variation in CYP2C19, CYP3A4A, CYP3A5, MDR1 and PON-1 genes were also evaluated.

Conclusion: Sustained release nitrate agent is a new determinant of clopidogrel hyporesponsiveness in patients with dual antiplatelet maintenance therapy.

Logistic regression analysis

<table>
<thead>
<tr>
<th>Variate</th>
<th>Multivariate logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (decade)</td>
<td>1.39 1.09–1.77 0.01</td>
</tr>
<tr>
<td>DM</td>
<td>1.57 1.00–2.47 0.05</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.47 0.26–0.82 0.01</td>
</tr>
<tr>
<td>LOF allele</td>
<td>3.08 1.99–4.76 -0.01</td>
</tr>
<tr>
<td>Nitrate</td>
<td>1.74 1.14–2.65 0.01</td>
</tr>
</tbody>
</table>

Multivariate logistic regression analysis for high PRU defined as 242 or more.

Conclusion: Sustained release nitrate agent is a new determinant of clopidogrel hyporesponsiveness in patients with dual antiplatelet maintenance therapy.
Clinical picture and mortality in cardiogenic shock in the contemporary era

Table 1. Independent predictors of in-hospital and 90-day mortality in CS

<table>
<thead>
<tr>
<th>Variable</th>
<th>In-hospital mortality</th>
<th>90-day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per year)</td>
<td>1.04 (0.99–1.09)</td>
<td>0.99 (0.93–1.07)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>3.2 (1.3–8.4)</td>
<td>0.02 (1.9–8.4)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>12.5 (2.0–77.4)</td>
<td>0.007 (14.2–21.0)</td>
</tr>
<tr>
<td>ACS</td>
<td>7.8 (1.9–32.5)</td>
<td>0.005 (4.0–12.3)</td>
</tr>
<tr>
<td>Confusion on admission</td>
<td>3.3 (1–29.0)</td>
<td>0.02 (2.8–12.7)</td>
</tr>
<tr>
<td>Blood lactate (per mmol/L sore)</td>
<td>1.4 (1.2–1.6)</td>
<td>&lt;0.001 (1.4–1.2)</td>
</tr>
<tr>
<td>LVEF (per % decrease)</td>
<td>1.06 (1.02–1.09)</td>
<td>0.001 (1.03–1.10)</td>
</tr>
</tbody>
</table>

Conclusion: Cardiogenic shock is still associated with high in-hospital mortality. Commonly most commonly due to ACS, other causes account for one-fifth of cases of CS. Despite early invasive treatment, ACS is strongly and independently associated with short-term mortality. Independent predictors of risk include common clinical variables.

Strategies to reduce in-hospital mortality in acute coronary syndrome complicated with cardiogenic shock: a nationwide cohort study

Background: Cardiogenic shock complicating acute coronary syndrome (ACS) is associated with a high risk of in-hospital mortality (IHM). However, limited studies investigated treatment strategies to reduce IHM among these patients.

Method: We evaluated patients with ACS and cardiogenic shock from the National Health Insurance Research Database (NHIRD) from 1997 to 2009. Cox regression analysis was used to find factors associated with IHM.

Results: Overall 1176 patients had developed cardiogenic shock during the index ACS hospitalization. Age was 71.4 (±9.0) years old and IHM rate was 65.6%. Average admission days were 10.37 (±3.6). There is no significant re-

duction in IHM rate between 1997 and 2009. Patients suffered from IHM are older, have more female, higher percentage of myocardial infarction, hypertension and use of angiotensin-II receptor blocker (ARB) and calcium channel blocker, less in-hospital use of clopidogrel, statin, heparin and glycoprotein IIb/IIa, lower percentage of diagnostic angiography and coronary revascularization but higher percentage of intra-aortic counterpulsation balloon use (IABP). Cox regression analysis showed age (hazard ratio [HR] 1.01, p < 0.001), myocardial infarction (HR 1.65, p < 0.01), heparin (HR 0.76, p < 0.01), clopidogrel (HR 0.76, p < 0.01), statin (HR 0.79, p < 0.05), coronary revascularization including percutaneous coronary intervention or coronary artery bypass graft (HR 0.60, p < 0.001), and intra-aortic counterpulsation balloon (IABP) (HR 3.26, p < 0.01) to be independent predic-
tors for IHM. Compared with those receiving all 4 treatments including heparin, statin, clopidogrel and revascularization, patients with above-mentioned 3, 2, 1 and 0 treatment had 1.99, 2.14, 2.54 and 2.86 folds of IHM risk, respectively (all p < 0.02).

Conclusion: Cardiogenic shock complicating ACS is still associated with high IHM rate under the contemporary care. Our results highlight the importance of evidence-based strategies including the antipatelet, anticoagulation, statin and coronary revascularization among the highest risk population.

Gender-related differences in outcome of patients with cardiogenic shock from acute myocardial infarction

Purpose: Women have been reported to have a higher incidence of cardiogenic shock after STEMI when compared to men. However, studies on gender-related differences in short-term and long-term outcome after cardiogenic shock have been reported less frequently. We investigated gender-related differences in out-

come of patients with cardiogenic shock from STEMI undergoing primary PCI.

Methods: A series of 544 consecutive patients admitted with cardiogenic shock from STEMI undergoing primary PCI were included between 2000-2012.

Results: A total of 138 (25.4%) patients were women and 406 (74.6%) were men. Women were significantly older (68.1 vs 62.3, p < 0.001), had a higher incidence of hypertension, a lower incidence of prior MI, and had lower serum creatinine and CK levels at admission. Women more often presented with inferior (vs. anterior) STEMI, but less often with out-of-hospital cardiac arrest. Women more frequently underwent PCI of the left main, but less frequently of the left anterior descending artery. Other baseline characteristics were similar. Thirty-day all-cause mortality was 50% in women and 35% in men (p < 0.001). All-cause mortality at 10-years of follow-up was 72% and 57%, respectively (Fig. 1, p < 0.002). After multivariable adjustment for differences in baseline variables, mortality in women remained significantly higher (OR for 30-day mortality 2.40 (95%CI 1.43-3.64) and HR for 10-year mortality 1.53 (95%CI 1.14-2.06).

Conclusion: Women admitted with cardiogenic shock from STEMI undergoing primary PCI had a substantially higher mortality that persisted after adjustment in multivariable analysis. This difference developed in the first 30 days and persisted during 10 years of follow-up.

Serum lactate in cardiogenic shock: clearance vs. single values – a biomarker substudy of the IABP-SHOCK II trial

Background: Serum lactate is widely used and an important biomarker for dis-
ease severity assessment in critically ill patients including those with cardiogenic shock (CS) complicating acute myocardial infarction. In sepsis and septic shock, lactate percentage of lactate reduction over time – the lactate clearance (LC) - has been extensively investigated. In CS only limited data are available.

Methods: In the randomized Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial 600 patients with CS complicating acute myocardial infarction undergoing early revascularization were assigned to therapy with IABP or no IABP. Lactate levels at baseline (L1) and after 8 hours (L2) were collected prospectively. LC was calculated for every patient (Figure 1). The areas under the
curves (AUC) of receiver operating characteristics for L1 vs. L2 vs. LC were compared with c-statistics for prediction of 30 day mortality. Youden index was used to gain best cut-off values. A multivariable Cox regression analysis for prediction of 30-day mortality was applied to assess possible independent impact for time to death prediction.

Results: For 529 of 600 patients (88.2%) L1 and L2 were consecutively LC values were available. The 30-day mortality in this cohort was 39.5% (209/529). The AUCs (L1: 0.67; L2: 0.76; LC: 0.62) showed no statistical difference between L1 and LC (p<0.20). In contrast, L2 AUC was significantly higher than for both other parameters (p<0.001, respectively). Youden index calculated 3.7 mmol/L as best cut-off value for L2. In multivariable stepwise Cox regression analysis L2 >3.7 mmol/L and LC < 3.25%/h remained independent predictive of time to death (p<0.001 for both) with L2 showing highest x²-score (103) and hazard ratio (3.03, 95% CI 1.95-4.66). 

Conclusion: L2 seems to be superior in prediction of death in comparison to L1 and LC. A cut-off value of 3.7 mmol/L for L2 after 8 hours showed the best discrimination for assessing early prognosis in CS.

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A simple score chart to assess risk of mortality at time of hospital admission for patients with cardiogenic shock from acute myocardial infarction


Purpose: Early risk stratification is important in patients with cardiogenic shock from STEMI. We aimed to develop a simple risk score that can be used at time of hospital admission to assess risk of 30-day mortality.

Methods: A series of 544 consecutive patients admitted with cardiogenic shock from STEMI who were intended to undergo primary PCI were included between 2000 and 2012.

Results: Overall 30-day mortality was 38.4% and did not change over the years (p-trend=0.64). Baseline variables known at time of hospital admission (including cardiac history, conventional risk factors, out-of-hospital cardiac arrest, physical examination, infarct location and serum lactate level) were entered into a logistic regression model in a forward stepwise manner. Only age (OR per category 1.45, 95% CI 1.25-1.69, p<0.001) and serum lactate level (OR per category 1.82, 95%CI 1.53-2.16, p<0.001) remained independent predictors of 30-day mortality, and were subsequently used to develop a score chart (left figure) that stratifies risk of 30-day mortality into categories ranging from 0-20% to 80-100%. The calibration plot (right figure) showed a close relation between the actual mortality rates in each risk category and the expected mortality rates obtained from the score chart. C-index of the model was 0.74. Adding information on the clinical course during intensive cardiac care unit stay, intra-aortic balloon pump support, cardiac markers, and variables obtained from coronary angiography and PCI did not significantly improve predictive accuracy of the model (c-index 0.77, p=0.32).

Conclusions: The outcome of patients with cardiogenic shock from STEMI can be largely predicted at time of hospital admission by a simple score chart that uses two variables, namely age and serum lactate level.

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Invasive vs. non-invasive ventilation and ventilatory parameters: do they predict outcome in cardiogenic shock

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Purpose: Despite scarce data, invasive mechanical ventilation (MV) is widely recommended over non-invasive ventilation (NIV) for ventilatory support in cardiogenic shock (CS). We analysed the role of ventilation strategies (VS) for in-hospital (I-H) outcome in CS.

Methods: 220 patients from the European CardShock study were categorized by maximal ventilatory support needed during the first 24 hours into MV and NIV groups. Clinical characteristics, treatment and outcome were analysed.

Results: Mean age was 66.6 years (SD 11.8), 73% were men. MV 134 (61%) and NIV 28 (13%) groups did not differ significantly in age, gender, medical history, etiology of CS, PaCO2/FiO2-ratio, baseline hemodynamics or LVEF. ACS was the main cause of CS (81% in MV and 79% in NIV group). 3 (2%) of MV group and was initially treated with NIV. After the first 24 hours 5 (18%) from NIV group got intubated.

Differences in laboratory and ventilatory parameters, length of hospital stay (LOS) and I-H mortality are shown in the table. MV group had significantly higher lactate level and greater need for vasoactive drugs referring to severe tissue hypoperfusion whereas NIV group seemed to be more congestive.

After adjusting for other predictors of outcome (age, history of CABG, systolic blood pressure, LVEF, lactate, ACS and need for adrenalin), mean 0-24 h FiO2 2.9 (2.5-4.08).

Conclusion: NIV seems a safe option for properly chosen CS patients. Interestingly, the ventilatory parameters, only mean 24-hour FiO2 independently predicted I-H mortality.

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Prasugrel vs. clopidogrel in cardiogenic shock patients undergoing primary PCI for acute myocardial infarction: results of the ISAR-SHOCK registry

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Purpose: Primary PCI is the recommended reperfusion therapy for patients with acute myocardial infarction (AMI) complicated by cardiogenic shock (CS). However, randomized data is lacking comparing different P2Y12 receptor inhibitors in this setting and current guidelines still favour the use of clopidogrel. The aim of the ISAR-SHOCK registry was to compare the clinical outcome of patients treated with clopidogrel vs. prasugrel in CS patients.

Methods: Patients (n=145) with AMI complicated by CS and undergoing primary PCI in two centers between January 2009 and May 2012 were included in this registry. The use of prasugrel for patients in this registry was triggered by an individual decision-making that also reflected platelet function testing results during the acute AMI phase. The primary endpoint was 30-day all-cause mortality. Secondary endpoints were stent thrombosis (ST) and TIMI bleedings at 30-days.

Results: With regard to antiplatelet treatment in the 145 CS patients, 50 patients were initially treated or immediately switched to prasugrel while 95 patients were treated with clopidogrel. All-cause mortality was lower in prasugrel vs. clopidogrel treated patients (30% vs. 50.5%, HR: 0.51, 95% CI 0.29-0.92, p=0.02, see Fig. 1). There was no difference for the occurrence of ST (HR: 2.95, 95% CI 0.27-32.68, p=0.38) or bleeding complications (combined TIMI major and minor bleedings, HR: 1.3, 95% CI 0.75-2.26, p=0.35).

Conclusions: Though MV is generally recommended, a fair number of patients were treated with NIV. Moreover, initial VS did not affect outcome. Thus NIV seems a safe option for properly chosen CS patients. Interestingly, the ventilatory parameters, only mean 24-hour FiO2 independently predicted I-H mortality.

Figure 1

Conclusion: Results of the ISAR-SHOCK registry suggest that the use of prasugrel in AMI patients complicated by CS might be associated with a lower mortality risk and a comparable safety profile as compared to clopidogrel therapy. Further studies are needed to determine the optimal antplatelet treatment regimen in this high-risk cohort of patients.
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Levosimendan to wean inotropic drugs in end stage heart failure patients

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Background: Despite mixed results in acute heart failure (SURVIVE, REVIVE), Levosimendan, a “calcium sensitizers” with a long half life, may have an interest in other clinical situation.

Purpose: To assess success rate of inotropic drugs withdrawal with Levosimendan in patient with end stage heart failure (HF) who previously failed weaning from inotropic agents.

Methods: Levosimendan was proposed to 16 end stage heart failure patients dependent of inotropic drugs between 2004 and 2013. Weaning success was defined as complete withdrawal of inotropic agents within 24 hours of intravenous infusion of levosimendan (0.1 μg/kg/min), transient success as the need to reintroduce inotropic agents within 24 hours after weaning and failure as the inability to stop inotropic agents. We also report 6-month survival rates, survival time, rates of exit from intensive care unit and home return.

Results: Mean age was 60 years old. Dilated cardiomyopathy was the leading cause of HF (50%). Mean heart rate was 90/min and blood pressure 100/62 under inotropic agents (dobutamine 94%). Mean NT-proBNP was 8658 ng/l. 17% had a creatinine Clearance=30 ml/min, 18% a factor V ≤50%.

Figure shows weaning success rate. Mean duration of weaning was 145±191 days. At 6 months, 50% of weaned vs. 13% of not weaned patients survived. Mean duration of weaning was 145±191 days. At 6 months, 50% of weaned vs. 13% of not weaned patients survived. In case of successful weaning (n=10), mean survival time was 216±224 days. Ninety percent of the patients could leave the intensive care unit and 30% get back home.

Conclusion: 24 hours intravenous infusion of Levosimendan allows weaning of more than half of end stage HF patients dependent on inotropic drugs. Despite a dramatic prognosis, weaning lasted 5 months and allowed 90% of patients to leave the intensive care unit and 30% to go back home.

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Diabetes mellitus prevents ischemic preconditioning in patients with reperfused acute myocardial infarction: insight from cardiovascular magnetic resonance


Background: Several studies suggest that preconditioning angina occurring shortly before the onset of acute ST-segment elevation myocardial infarction (STEMI) is associated with favorable outcomes by the mechanism of ischemic preconditioning. And more, recent studies demonstrated that such beneficial effects of preconditioning angina were not observed in diabetic patients. Non-invasive quantitative assessment of microvascular obstruction (MVO) by cardiovascular magnetic resonance (CMR) provides a specific biomarker of severe microvascular dysfunction. The aim of this study was to determine whether preconditioning angina was related to the presence of severe microvascular dysfunction determined by CMR in patients with acute STEMI.

Methods: The study population consisted of 202 consecutive patients with a first STEMI successfully treated with primary percutaneous coronary intervention (PCI): 161 patients without diabetes and 41 patients with non-insulin treated diabetes mellitus. Preconditioning angina was defined as angina occurred 24 to 72 hours before the onset of infarction. Late gadolinium-enhanced (LGE) CMR performed within 4 days after primary PCI was used to measure MVO.

Results: Patients with MVO were more frequently observed in patients without angiogenic shock and to reduce vasopressor need. Even in patients after cardiac arrest is might be reasonable because it re-constitutes circulation faster and more effectvily than under pure inotropic stimulation. Device-associated complications are rare and mainly required improved bleeding management.

Cardiogenic shock has a high mortality, and catecholamines traditionally used to stabilize blood pressure are increasingly recognized to have unfavorable side effects. Therefore attention is directed on mechanical hemodynamic support. We want to report on safety, efficacy and handling of the percutaneous implantable microaxial Impella-pump in our institution.

Methods: First 36 patients were evaluated (28 male, 8 female, mean age 66.4 years (42-84)). Indication for hemodynamic support was: high-risk coronary intervention (n=5, “elective”), during or shortly after cardiac resuscitation (n=17, “CPR”) and acute myocardial infarction with cardiac shock (n=14, “shock”). All patients had PCI. Hemodynamic data and medical reports were retrospectively analysed.

Results: Hemodynamic support with the Impella system was provided for an average of 54.8 hours (1.5-128 h). At implantation patients were highly catecholamine dependent, but within 2h vasopressor doses dropped significantly (e.g. in a preliminary analysis of n=16 pat. from norepinephrine mean 128.2 μg/h to 18.9 μg/h, accompanied by lactate decrease indicating better organ perfusion. Enzyme course reflects shock in general as well as cardiac damage. Several patients had acute renal failure, renal replacement therapy was needed by 13. Difficulties related to the device mainly consisted of hemolysis and bleeding, both because of compromised plasmatic coagulation and problems at puncture site. Therefore transfusion was necessary on average of 7.4 erythrocyte concentrates (CPR) resp. 4.8 (shock group), in contrast only 0.5 in elective patients. CPR patients also needed 3.9 units of fresh frozen plasma, in shock 1.6, n=6 resp. 3 were given thrombocytes and n=6 additionally PPSB.

In several patients reposition of the device was necessary. 1 woman with peripheral artery disease and prior implantation of a dacron prosthesis had surgical vessel closure. In the elective group one patient died within 30 days after an consecutively planned CABG operation. In the shock group n=11 had survival to discharge with at least 5 still were alive 30 days later. In the CPR group however 12 patients died of progressive multiorgan failure, 1 because of ventricular rupture. Conclusion: Use of the Impella-device can help to stabilize patients in cardiogenic shock and to reduce vasopressor need. Even in patients after cardiac arrest is might be reasonable because it re-constitutes circulation faster and more effectively than under pure inotropic stimulation. Device-associated complications are rare and mainly required improved bleeding management.
angina occurred 24 to 72 hours before infarction compared to those with the preinfarction angina (65% vs 38%, p=0.033). In non-diabetic patients, preinfarction angina was associated with smaller sizes of LGE and MVO (13.4±9.6 vs 21.9±12.6% of left ventricle, p=0.0005; 0.8±1.4 vs 2.6±3.3% of left ventricle, p=0.0037, respectively). On the contrary, in diabetic patients, there was no significant difference in the total sizes of LGE and MVO (11.7±14.1 vs 21.6±14.0% of left ventricle, p=0.1149; 1.7±2.7 vs 3.4±5.1% of left ventricle, p=0.4236, respectively) between patients with and those without preinfarction angina.

**Conclusion:** Preinfarction angina limited infarct and MVO size in non-diabetic patients with STEMI. However, such beneficial effects of preinfarction angina were not observed in diabetic patients, suggesting that diabetes might prevent ischemic preconditioning.

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**1949 | BEDSIDE**

Does the localization of ischemia in patients who undergo dobutamine stress cardiac magnetic resonance imaging influence outcome?

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**Aims:** To evaluate the impact of ischemia localization for the prediction of hard cardiac events in patients with known or suspected CAD who undergo dobutamine stress cardiac magnetic resonance imaging (DCMR). 

**Methods:** 3166 patients (pts.), 63±12 years, 27% female underwent DCMR. Pts. were grouped in 3 coronary artery territory of stress induced wall motion abnormalities (WMA) using the AHA/ACC/ESC standard. Pts who showed WMA in only one territory were further analyzed. Cardiac death and nonfatal myocardial infarction were registered as hard cardiac events. Pts with an “early” revascularization procedure (in the first three months) were not included in the final survival analysis.

**Results:** Pts. were followed for a median of 3.1 years (interquartile range 2.4-4.5 years). 187 (5.9%) pts. experienced hard cardiac events. 613 pts (19.4%) had inducible ischemia in only one coronary territory (32.1% LAD, 37.4% LCX, 30.5% RCA) and were further analyzed. Pts with inducible ischemia in the LAD territory had a higher rate of hard cardiac events compared to other territories (HR=2.5, 95%CI=1.4-4.4, y2=18.1, p<0.001, HR LAD vs. LCX=2.7, 95%CI=1.4-5.3, HR LAD vs. RCA=3.3, 95%CI=1.5-7.4). No difference in the likelihood of hard cardiac events was noted between RCA and LCX territories (HR=0.8, 95%CI=0.4-1.5) (see figure). In the first three years, inducible ischemia in the LAD territory was associated with a yearly event rate of ~10%, in comparison to ~4% seen in those with inducible ischemia in non_LAD territories (p<0.001).

**Conclusions:** The presence of inducible ischemia in the LAD territory is associated with a higher rate of cardiac events compared to other territories in patients with known or suspected coronary artery disease.

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**1950 | BEDSIDE**

Cardiac magnetic resonance based management of coronary artery disease at 3.0 Tesla: insights from a large single center experience


**Background:** Cardiac magnetic resonance (CMR) has become a robust diagnostic tool for the assessment of coronary artery disease (CAD). However, little is known about the role of CMR at 3.0 Tesla for guiding management of CAD. This study was therefore aimed to describe the role of stress-perfusion/viability CMR at 3.0 Tesla for guiding the clinical management of a large and heterogeneous collective of patients with known or suspected CAD.

**Methods:** This was an observational single center study. Consecutive patients (n=847) undergoing stress / viability CMR on a 3.0 Tesla system at our institution were stratified according to CMR findings of myocardial ischemia and scar, and followed for clinical events. Multiple aspects such as appropriateness of CMR-driven coronary angiography (cath) in ischemia positive patients, diagnostic accuracy of stress-perfusion CMR into a coronary territory analysis and its prognostic value were described.

**Results:** Myocardial scar was detected in 298 patients (35%) and ischemia in 214 patients (25%). Among patients with evidence of myocardial ischemia, 126 (59%) underwent CMR-driven cath. The ischemic score was significantly higher in patients undergoing cath as compared with patients followed conservatively in spite of myocardial ischemia (median [IQR] 4 [2-5] vs 2 [1-3]; p<0.001). Events rate of cardiac death or non-fatal myocardial infarction were significantly lower in patients without myocardial ischemia or scar as compared to others (rate per 100 person/year [95% CI] – 0.23 [0.03 - 1.62] vs. 2.30 [1.20 - 4.42]; p=0.036). The same was true for the combined endpoint of cardiac death, non-fatal myocardial infarction and need of coronary revascularization (rate per 100 person/year [95% CI] – 1.85 [0.93-3.70] vs. 38.39 [31.87-46.25]; p<0.001). For the latter end-point, CMR findings added incremental prognostic value as compared with clinical data only (Likelihood ratio test, p=0.001). Sensitivity and specificity of CMR at detecting a significant coronary lesion (~50% stenosis) were of 74% and 87%, respectively, resulting in a 94%-rate of CMR-driven cath in ischemia positive patients being clinically appropriate (i.e. evidence of ~50% stenosis and/or revascularization needs).

**Conclusion:** CMR guided management of CAD at 3.0 Tesla is associated with a very good diagnostic accuracy at detecting significant CAD, an efficient downstream utilization of cath and a very good cardiac prognosis.
ISI also improved significantly, after PCI (basal ISI 21±10.2% vs. post-PCI ISI 4±7.0%, p<0.001). The distance walked in the six-minute test improved at follow-up (431±111.5 meters pre-PCI vs. 458±110.4 meters post-PCI, p=0.050). Moreover, chest pain after the six-minute walk test significantly decreased post-PCI (p<0.001).

Patients with ISI >20% before PCI (n=19) showed a significant improvement in the six-minute walk test at follow-up (basal distance walked 440±197.1 meters vs. follow-up distance walked 487±83.6 meters, p=0.041) that was not observed in those patients with ISI <20% (444±102.1 vs. 437±115.0 meters, p=0.718).

Conclusion: Successful CTO PCI leads to a reduction in inducible myocardial ischemia assessed by CMR. The improvement in the functional status, measured by the six-minute walk test, is only statistically significant in those patients with the highest ischemic burden at stress CMR, suggesting that improvement of clinical status parallels the degree of relief of ischemia.

**IMPROVING OUTCOME WITH CARDIAC RESYNCHRONISATION THERAPY: STILL A CHALLENGE**

**2045 | BEDSIDE**

A resynchronization optimization clinic improves survival and response of heart failure patients treated with resynchronization therapy

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**Background:** Cardiac resynchronization therapy (CRT) improves symptoms and survival in patients with heart failure (HF). However, a large number of patients do not respond to CRT. We aim to evaluate the effect of a resynchronization optimization clinic (ROC) on the outcome and response of patients receiving CRT.

**Methods:** We compared outcomes of consecutive patients receiving CRT with standard care (SC) and patients followed by a resynchronization optimization clinic (ROC). Patients were followed prospectively in an integrated team consisting in a heart failure specialist and an electrophysiologist. Clinical assessment, echocardiography, functional test and quality of life were routinely performed at baseline, 6 and 12 months follow-up. A proportional hazard Cox regression model adjusted by propensity scores (based on age, ejection fraction, ischemic cardiomyopathy, atrial fibrillation, creatinine and functional class) was applied to estimate the hazard ratio and 95% confidence interval.

**Results:** A total of 582 patients were included in the study with a mean follow-up of 3.7±2.5 yrs, 258 pt in the SC group and 324 in the ROC group. Patients in the SC group were older (68±1.8 vs 66±2.1 y, p=0.001) and had worse creatinine (1.4±0.5 vs 1.2±0.5, p=0.04). After adjustment for these differences, ROC was associated with a lower hazard for overall mortality (HR 0.55, 95% CI: 0.4-0.8, p<0.001) and cardiovascular mortality (HR 0.45, 95% CI: 0.3-0.7, p<0.001). Clinical responder rate at twelve months follow-up was significantly higher in the ROC group (74% vs. 67%, p=0.04).

**Conclusions:** Follow-up by a CRT optimization clinic may improve overall and cardiovascular survival and increase responder rate in HF patients treated with cardiac resynchronization therapy.

**2046 | BEDSIDE**

Age-specific mortality and hospital readmission risks following CRT implantation - a nationwide study

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**Purpose:** Cardiac resynchronization therapy (CRT) is recommended in patients with appropriate indications and survival expected to exceed one year. We aimed to evaluate mortality and hospital readmission rates in CRT-recipients according to age-categories in an unselected nationwide population.

**Methods:** From nationwide Danish health registers we identified all patients ≥40 years receiving first-time implantations of a CRT-device during 2000–2010 with multi-site pacing alone (CRT-P) or with implantable cardiac defibrillator (CRT-D).

According to age-categories ≥50 years, 50-59 years, 60-69 years, 70-79 years and ≥80 years, rates of all cause mortality and incidence rates of hospital readmission did not vary. Although mortality rates increased with advancing age, the mortality risks were comparable across age-categories (Table). In patients receiving a CRT-P, age-adjusted cardiovascular readmission rates per person-year were 0.9 for 50-59, 0.8 for 50-59, 0.9 for 60-69, 0.8 for 70-79 and 0.8 for patients ≥80 years old. Corresponding age-adjusted mortality rates per person-year for patients receiving a CRT-D were 1.6 for ≤50, 1.5 for 50-59, 1.2 for 60-69, 0.9 for 70-79, and 1.2 for patients ≥80 years old.

**Conclusions:** In an unselected nationwide population over a time period encompassing the first decade of CRT implantation, 30-day and one-year mortality risks were low across all age-groups, but increased with age. In particular in CRT-P patients. Cardiovascular hospital readmissions were comparable across all age groups.

**2047 | SPOTLIGHT**

Combination of cardiac resynchronization and cardioverter defibrillator for heart failure with reduced ejection fraction: a network meta-analysis

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**Purpose:** We intended to conduct this network meta-analysis to compare the efficacy of cardiac resynchronization therapy (CRT)-defibrillator (CRT-D) with CRT-pacemaker (CRT-P) or implantable cardioverter defibrillator (ICD) in reducing mortality among patients with heart failure with reduced ejection fraction (HFrEF). We intended to compare any randomized controlled trials comparing CRT-D, CRT-P and ICD in patients with HFrEF identified through relevant databases. We performed Bayesian network meta-analyses to compare the efficacy of these therapies in the reduction of all-cause death, sudden cardiac death (SCD), heart failure death, and non-cardiac death.

**Methods:** Thirty eligible trials with 16553 participants were identified. Compared with medical therapy, CRT-D significantly reduced all-cause death (OR 0.65, 95% CI 0.46-0.88) and SCD (OR 0.34, 95% CI 0.21-0.51). CRT-D trended to reduce all-cause death over ICD. When compared with CRT-P, CRT-D trended to reduce all-cause death and significantly reduced SCD (OR 0.40, 95% CI 0.21-0.65) however trended to increase heart failure death and non-cardiac death. Sensitivity analysis revealed that CRT-D significantly reduced all-cause death (OR 0.77, 95% CI 0.61-0.97) and heart failure death (OR 0.72, 95% CI 0.50-0.96) over ICD after exclusion of trials studying patients with narrow QRS complex.

**Conclusions:** Among patients with HFrEF, CRT-D exhibited superiority over ICD only in patients with prolonged QRS duration. Current evidence is insufficient to support significant superiority of CRT-D over CRT-P. The clinical indications of
this expensive device might deserve more deliberation to target proper patient population.

2048 | BEDSIDE
Prevalence of “TRUE LBBB” in current practice of CRT implantation
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Aim: New stricter criteria for complete LBBB definition were recently proposed. The aim of this study was to describe the current clinical practice associated with CRT implantation and how the adoption of stricter criteria for patient selection could modify recommendation classes.

Methods: We collected data from 514 consecutive patients who underwent CRT implantation from 2011 to 2013 in 35 centers. All baseline ECG were centrally reviewed in order to assess the presence of mid-QRS notching or slurring and measure the QRS duration in any leads. Indications to CRT were categorized into recommendation classes, according to current guidelines for patients in sinus rhythm: Class I in presence of LBBB (Level A with QRS duration >150ms and Level B with QRS duration 120-150ms), Class IIa Level B with no-LBBB and QRS duration >150ms and Class IIb Level B with no-LBBB and QRS duration 120-150ms. All recommendations require chronic heart failure patients with LVEF ≤35%, and NYHA functional class II, III or ambulatory IV despite adequate medical treatment.

Results: Baseline characteristics were: mean age 70±10 years, male gender 72%, ischemic etiology 44% and history of atrial fibrillation 30%. Almost all patients were in NYHA class II or III (32% and 64%, respectively). An LBBB was present in 84% of patients, while 7% had an RBBB, 8% an incomplete bundle branch block and 1% a non-specified IVCVD. 41% of patients met Class I Level A recommendation, 33% Class I Level B, 7% Class IIa Level A and 5% Class IIb Level B. The remaining 14% of patients were in atrial fibrillation or had a pacemaker indication. Among patients with LBBB, 73% had mid-QRS notching or slurring in at least one lead and a QRS >120ms. Notching or slurring was also present in 30% of patients with a QRS <120ms. According to the novel definition, “true LBBB” was confirmed in only 39% of LBBB patients (36% male, 46% female). Therefore, 19% of Class I Level A recommendations could be reclassified as Class IIa Level B, and 32% of Class IIb Level B as Class IIb Level B.

Conclusion: Patients with complete LBBB may benefit the most from CRT, thus distinguish the LBBB from other conduction disorders may be clinically relevant. Novel and more specific criteria for LBBB detection, if applied in current clinical practice, may significantly impact the level of recommendation for CRT. The analysis of long-term results will clarify whether more specific selection criteria could be associated with better outcome.

2049 | BEDSIDE
Post-CRT implant electrocardiographic score as a predictor of clinical outcome
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Background: Optimal left ventricular lead position and device programming are determinants of cardiac resynchronization therapy (CRT) response. Our study examined the ability of a simple scoring system using the post-CRT implant 12-lead ECG to predict clinical outcome.

Methods: We retrospectively analyzed ECGs of consecutive patients undergoing CRT implantation and followed up in our multidisciplinary clinic. ECG parameters: i) QRS duration, ii) time to intrinsoid deflection onset (ID) and iii) voltage change in V1 lead was measured on the post-implant ECG and compared to pre-implantation parameters. Clinical outcome was assessed as a composite of all-cause death, LVAD implantation, cardiac transplantation and HF hospitalization.

Results: EKG of 487 patients were evaluated. Better survival was predicted by i) shortening of QRS duration ≥20 msec (HR 0.65 [95% CI 0.48-0.87] p<0.008), ii) 50% decreased summed voltage in V1 lead (0.67 [0.49-0.90] p=0.008) and iii) ≥40 msec ID time in V1 after pacing (0.63 [0.46-0.87] p<0.005 in univariate analysis). Each positive ECG variable was given a numerical value of 1 to create the score ranging 1-3. The scoring system had a significant graded trend towards predicting the clinical outcome (Fig. 1, p<0.001).

Conclusion: The post-CRT 12-lead ECG score can predict long-term clinical outcomes. Prospective intra-procedural use of this scoring system to facilitate individualized LV lead placement needs evaluation.

2050 | BEDSIDE
Impact of long-term clinical outcomes of upgrading from chronic right ventricular pacing to cardiac resynchronization therapy in patients with heart failure
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Background: Patients with chronic right ventricular (RV) pacing upgraded to cardiac resynchronization therapy (CRT) have been excluded from majority of clinical trials of CRT. There remains to be seen whether upgrade to CRT is effective in patients with chronic RV pacing.

Purpose: To determine long-term clinical outcomes of upgrading from chronic RV pacing to CRT.

Methods and results: CUBIC study is a multi-center registry of patients undergoing upgrade to CRT from chronic RV pacing to CRT (RVP: n=221) or primary CRT implantation (Non-RVP: n=724). Compared with Non-RVP, RVP patients were older (71 years vs. 69 years, p=0.002) and more likely to be female (38% vs. 28%, p=0.006) and to have wider QRS width (160 ms. vs. 147 ms., p<0.0001), chronic atrial fibrillation or flutter (32% vs. 19%, p<0.0001) and non-ischemic etiology (83% vs. 66%, p=0.0001). The prevalence of diabetes, chronic kidney disease (CKD) and severe mitral regurgitation were similar between RVP and Non-RVP groups (at 3 years, death: 79.0% vs. 78.3%, log rank p=0.71; hospitalization for HF: 68.4% vs. 65.1%, p=0.19; CE: 60.5% vs. 56.5%, p=0.34, respectively). There was also no significant difference in the rate of reverse left ventricular remodeling defined as left ventricular end-systolic volume reduction ≥15% after 6 months (RVP: 63% vs. Non-RVP: 59%, p=0.37) and in the clinical responder rate defined as an improvement (≥1 score) of NYHA class after 6 months (RVP: 62% vs. Non-RVP: 66%, p=0.31). By Cox hazard models, the RVP was not significantly associated with an increased risk of CE relative to the Non-RVP: hazard ratio (HR) 1.09, 95% CI 0.84-1.41. Among RVP patients, independent predictors of CE were CKD (HR 1.78 95% CI 1.09-2.85), shorter duration (>5 years) of RV pacing before upgrade (HR 1.63, 95% CI 1.03-2.62) and use of ACE inhibitors or ARBs (HR 0.46 95% CI 0.29-0.73) and diuretics (HR 2.53, 95%CI 1.20-6.05). Three-year survival rate was comparable between those upgrading to CRT plus ICD and those to CRT alone (75.7% vs. 81.7%, respectively, p=0.32).

Conclusions: Long-term clinical outcomes were similar in patients undergoing upgrade to CRT from chronic RV pacing to those undergoing primary CRT.

PREDICTION AND PREVENTION OF ATRIAL FIBRILLATION
P2053 | SPOTLIGHT
Association between left atrial size and future atrial fibrillation: A 16 year follow up of 2369 women and men. Tromso study 1994-2010
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Purpose: Atrial fibrillation (AF) increases the lifetime risk of stroke and heart failure. Several risk factors of AF have been identified. The purpose of this study was to investigate the association between echocardiographic measurements with emphasis on left atrial (LA) size and future risk of incident AF in a large population-based cohort.

Methods: A random sample of 2369 participants in the Tromso study in Northern Norway who were 50 years and older and without AF at baseline were followed from 1994 to 2010. LA size was indexed by body surface area (BSA) and was categorized into three groups as normal (<2.2 cm²/m²), moderately (2.2-2.7 cm²/m²) and severely (>2.8 cm²/m²) enlarged. To estimate sex-specific hazard ratios (HRs) for AF we used both age-adjusted and multivariable Cox proportional
hazards regression models adjusted for age, systolic blood pressure, heart rate, body mass index, BSA, total and HDL cholesterol, and self-reported use of alcohol, smoking, coffee, physical activity, hypertension, prevalent coronary heart disease (CHD) and diabetes.

**Results:** Mean age at baseline was 62.6 years and 51.4% were women. During follow-up we identified 462 cases of incident AF (193 women). LA size was associated with AF in both sexes. A moderately enlarged LA was in both women and men associated with 64% increased risk for AF compared to subjects with normal LA size. In subjects with severely enlarged LA, we found HRs for AF of 4.4 (95% CI, 2.6-7.4) in women and 3.9 (95% CI, 2.7-7.8) in men compared with subjects with normal LA size (p-value for linear trend <0.001). Hypertension increased risk of AF (HR 1.6, 95% CI, 1.3-1.9) in age and sex adjusted analysis. This relationship was somewhat weaker (HR 1.5, 95% CI, 1.2-1.9) with additional adjustment for LA. Sex, LA size was in age and sex adjusted analysis of associated with AF (HR 2.4, 95% CI, 1.9-3.0). When also adjusted for LA size, the HR was slightly attenuated (HR 2.2, 95% CI, 1.7-2.9).

**Conclusion:** Enlarged LA size was independently associated with an increased risk of future AF in both sexes.

### P2054 | BEDSIDE

**A new biomarker based risk score for predicting major bleeding in atrial fibrillation - the ABC (age, biomarkers, current disease) risk score**

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**Purpose:** The benefit of oral anticoagulation in atrial fibrillation (AF) is based on a balance between reduction in ischemic stroke and increase in major bleeding. To improve the prediction of bleeding we developed a new risk score based on ABC biomarkers and clinical variables.

**Methods:** The study included 14,537 patients with AF randomized to either warfarin (target INR 2.0–3.0) or apixaban 5 mg b.d. in the Apixaban for Reduction in ISchemic Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTE) trial. Blood biomarkers reflecting cardiovascular and renal function – high sensitivity cardiac troponin (cTn-t), natriuretic peptide (NT-proBNP), growth differentiation factor 15 (GDF-15), cystatin-C, and hematocrit – were determined in randomization.

The biomarker levels and available clinical variables were assessed in Cox regression models predicting major bleeding where each variable with a relevant contribution to the c-statistic obtained a weight proportional to the Cox-model coefficients.

**Results:** The Cox-models were based on 25,150 person years of follow-up and 662 major bleeding events. The most important predictors were: GDF-15, cTn-t, hematocrit, and prior bleeding. The score obtained the acronym ABC (Age, Biomarkers (GDF-15, cTn-t, and hematocrit), Current disease (history of bleeding)). The ABC score yielded c-index 0.68, considerably higher than the conventional HAS-BLED score with c-index 0.59 in the same cohort. The net reclassification improvement was positive for the ABC risk score and yielded a significant improvement of 25% (p <0.001) as compared with HAS-BLED. The ABC score also achieved higher c-index compared with HAS-BLED in subgroups e.g. with no prior major bleeding (0.68 vs. 0.58, respectively), or only on warfarin (0.72 vs. 0.61, respectively). There were no differences in bleeding with apixaban compared with warfarin across the range of the ABC score.

**Conclusions:** A novel and simplified risk score for predicting major bleeding using biomarker and clinical data was developed from a large cohort of patients with atrial fibrillation on anticoagulation. The ABC bleeding risk score performed better than the currently guidelines recommended risk score and may lead to improved treatment decisions in patients with AF.

### P2055 | BEDSIDE

**Aerobic interval training reduces the burden of atrial fibrillation**

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**Purpose:** This study examines the influence of physical activity at different ages and on different type of the risk of developing AF in a large cohort of Swedish women.

**Methods:** Information about physical activity (PA) was obtained from 36 513 AF-free women (mean age 49–83 years, mean age 60 years) who had completed a self-administered questionnaire at baseline in 1997. Participants reported their time spent on leisure-time exercise (moderate to high-intensity PA) and on walking or bicycling (low- to moderate-intensity PA) throughout their lifetime (at 15, 30, and 50 years of age, and at baseline). Participants were followed up in the Swedish National Inpatient Register for ascertainment of AF. Cox proportional hazards regression models were used to estimate relative risks (RR) with 95% confidence intervals (CI), adjusted for potential confounders.

**Results:** During a median follow-up of 11.0 years (SD 2.4), 2915 cases of AF were diagnosed. Walking/bicycling at baseline was inversely associated with risk of AF (RR 0.81, 95% CI, 0.72-0.92, for >40 min/day vs. almost never). As little as 20-39 min per day of walking or bicycling showed a reduction in the risk of AF (RR 0.86, 95% CI, 0.76-0.97). Results were similar for walking/bicycling at age 50 years. Leisure-time exercise at baseline was also inversely associated with risk of AF (RR 0.85, 95% CI, 0.75-0.95 for >4 h/week vs. <1 h/week). There was no association between risk of AF and leisure-time exercise or walking/bicycling at the age of 15 and 30.

**Conclusion:** In middle-aged and elderly women, fairly small amounts of daily walking or bicycling were associated with a reduced risk of AF. Leisure-time exercise of more than four hours a week also showed a reduction in the risk of AF.

### P2057 | BEDSIDE

**Mineralocorticoid receptor blockade added on standard antiarrhythmic therapy decreases the atrial fibrillation recurrences in a 24 months study**

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**Purpose:** The alterations of atrial structure induced by the iterative atrial fibrillation (AFib) includes RAAS overexpression which could have a decisive role, aldosterone being involved in inflammation, fibrosis, remodelling. The objective of our study is to compare directly two therapeutic regimens (each with 3 sub-regimens) in order to assess the benefit of mineralocorticoid receptor blockade (MCRB) in repetitive AFib patients (pts).

**Method:** The study considered 1152 pts with AFib, starting from 1st Nov 2007, structured into two comparative groups, small male and 6th decade pts predominance. The pts within the first group were treated with antiarrhythmics (amiodarone (A) 69.6%, or propafenone (P) 22.65%, and sotalol (S) 7.66%). Prediction and prevention of atrial fibrillation 357

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P2058 | BEDSIDE

The effects of reactive antialtiractacyardia pacing on the progression of atrial tachyrhythmias: secondary analysis results of the randomised MINERVA trial

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Purpose: Atrial fibrillation (AF) is a frequent comorbidity in pacemaker patients. The MINERVA trial demonstrated that combining advanced pacemaker features that minimize unnecessary right ventricular pacing (MVP), atrial overdrive pace, and atrial tachycardia pacing at arrhythmia onset and during rhythm change (Reactive A TP) reduces permanent AF risk by relative 61% compared to standard dual-chamber pacing (DDDVR). We investigated Reactive A TP’s role on delaying atrial tachyrhythmia (AT/AF) disease progression in the MINERVA trial patients.

Methods: Dual-chamber pacemaker patients with AT/AF history were randomly assigned to receive DDDR (n=385), MVP alone (n=398), or the advanced features (DDDVR+MVP; n=383). Permanent AF or complete heart block were exclusion criteria. The primary outcome of this analysis was risk of persistent AT/AF, defined as ≥7 consecutive days with AT/AF. Secondary endpoints comprised AT/AF rate and Reactive A TP efficacy, adjusted via the generalized estimating equations (GEE) method. Persistent AT/AF incidence was estimated through Kaplan-Meier method. Associations with persistent AT/AF risk were evaluated via multivariable Cox regression.

Results: At baseline, 982 (86%) patients had history of AF, 228 (20%) history of atrial flutter, and 197 (17%) history of atrial tachycardia. Within 2 years of follow-up, 804 (69%) patients suffered AT/AF episodes and were characterized by a median AT/AF rate of 244 beats per minute (bpm), 25th-75th percentile range=216 bpm-280 bpm. GEE adjusted Reactive A TP efficacy was 44.5% (95% confidence interval=41.3%-47.6%). Reactive A TP efficacy was significantly and inversely associated with AT/AF rate, with a success rate of 35% for AT/AF rates > 340 bpm, 47% for AT/AF rates between 240 bpm and 340 bpm and 50% for AT/AF rates ≤240 bpm. The 2 years persistent AT/AF incidence (95% confidence interval) was 26% (22%-31%) in DDDR, 25% (21%-30%) in MVP and 15% (12%-20%) in DDDR+MVP (p=0.001 vs DDR, p=0.002 vs MVP). Multivariable modeling identified high Reactive A TP efficacy (-44.4%) as a significant predictor of reduced persistent AT/AF (hazard ratio (95% confidence interval)=0.42 (0.21-0.83), p=0.013).

Conclusions: In bradycardia patients, DDDR+MVP pacing delays AT/AF disease progression, with Reactive A TP efficacy being an independent predictor of persistent AT/AF reduction. While at baseline most of patients had history of AF, pacemaker diagnostics showed that most atrial arrhythmias started as atrial tachycardia and atrial flutter or, over time, transitioned to longer cycle lengths becoming subject to pace termination.

P2059 | BEDSIDE

Left atrial appendage closure/amputation did not affect the incidences of early post-operative atrial fibrillation occurrence or stroke: analysis based on post-operative echocardiographic examinations

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Purpose: Atrial fibrillation (AF) is the most common cardiac arrhythmia which is highly associated with morbidity and mortality, and its incidence after cardiac surgery has been reported to be 20-30%. The most relevant complication of AF is a significant increase in the risk of stroke. Since the left atrial appendage (LAA) is the main source of emboli, LAA closure or amputation in patients with chronic AF has been performed. However, the effect of LAA closure in patients without AF history on post-operative new-onset AF has not yet been elucidated. In the present study, we investigated how surgical LAA closure or amputation affect early post-operative new-onset AF and stroke.

Methods: We analyzed 1856 consecutive patients (69.2% of male, mean age 66.8±12.2 years-old) undergoing open-heart surgery between January 2009 and October 2013 at our institution. Among those, 805 cases (43.4%) underwent left atrial appendage closure (LAA-C) and 1051 cases (56.6%) received valvular surgery (V) and 246 cases (13.3%) undergoing combination of CABG and valvular surgery (CABG+V). The early post-operative clinical courses including paroxysmal AF occurrence between patients with and without concommitant LAA closure/surgery were compared.

Results: A total of 375 patients (20.2%) received LAA procedure. The incidence of post-operative AF was higher in patients undergoing LAA procedure as compared with those without the procedure (48.5% vs. 39.0%, p=0.0008); however in a subset of patients underwent CABG+V, the AF occurred less frequently in patients underwent LAA procedure (40.0 vs. 54.7%, p=0.0416). The incidence of stroke was not significantly different between those with and without LAA procedure (3.7% vs. 3.0%, p=0.4933). Multivariate analysis including pre-operative clinical characteristics, echocardiographic parameter, LAA procedure (yes=1, no=0) and surgery type (valvular=1, others=0) revealed that older age (years) (odds ratio (OR) 1.04, 95% confidential interval (CI) 1.01-1.05) and larger LA diameter (cm) (OR 1.05, 95%CI 1.03-1.06) were associated with AF development; however, neither LAA procedure or surgery type did not predict AF. The bleeding amounts, length of hospitalization, LAA closure/amputation were not significantly different between patients with and without LAA closure/amputation.

Conclusions: LAA closure/amputation at the time of open heart surgery can be safely performed; however, it did not affect early post-operative incidences of AF development or stroke. Further investigation would be required to evaluate its long-term efficacy on preventing stroke.

NON-PHARMACOLOGICAL ISSUES IN ADVANCED HEART FAILURE

P2060 | BEDSIDE

Predictors and late incidence of persistent or recurrent heart failure after aortic valve replacement for aortic stenosis compared with aortic regurgitation

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Aim: 1. To evaluate the effect of aortic valve replacement (AVR) on long term evolution of the left ventricular (LV) systolic and diastolic performance, comparing patients (pts) with aortic stenosis (AS) to pts with aortic regurgitation (AR). 2. To identify the independent predictors for persistence or recurrence of the congestive heart failure (HF) late after isolated AVR.

Methods: 10 years prospective study on 802 pts undergoing AVR for AS (456pts) or AR (346pts). Pts were evaluated clinically and echocardiographically (including TDI) preoperatively and yearly till 10 years postoperatively. The effect of demographic, morbiditary, and valve-related variables on the composite outcome of NYHA class III/IV symptoms or congestive heart failure death after surgery was determined with stratified logistic regression. Cox proportional hazard models and logistic regression. Multivariable analyses were adjusted for age and gender and included left ventricular ejection fraction (LVEF)<35%, restrictive left ventricular diastolic filling pattern (LVDPF), renal insufficiency and logistic EuroSCORE II (n=17) were included in multivariable analysis. 3. To evaluate the predictors postoperative AR (25.1%), LA dimension index (LA المستمر 37.19% of pts as score group and at 65.79% pts from AR group. Also, LVEF<35% was found at 21.95% pts from AS group and at 56.52% pts from AR group.

Conclusions: 1. LV systolic and diastolic dysfunction is reversible mostly after AVR for AS than for AR, both in the early and late postoperative term. 2. On long term, freedom from congestive HF or cardiovascular death was significantly higher in AS group. The presence of restrictive LVDPF had a significant impact on outcomes, decreasing long-term survival and increasing hospitalization rates, mostly in preoperative AR. 3. The main predictors for persistence or recurrence of HF late after AVR were: preoperative AR, restrictive LVDPF, LA dimension index <30mm/m2, LVEDV >200cm3, preoperative NYHA class IV (RR=9.2), atrial fibrillation (AF) (RR=6.2), obstructive pulmonary disease (COPD) (RR=28.6), smoking (RR=18.7), prosthesis mismatch (RR=12.5) and 2 degree mitral regurgitation (RR=4.0) (p<0.05).
P2061 | BEDSIDE
Long-term prognostic role of Ca-125 in non-congestive patients undergoing cardiac transplantation

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Introduction: Carbohydrate antigen 125 (Ca-125) is a well-established biomarker for monitoring ovarian cancer growth. Recent studies have suggested that Ca125 serum levels are remarkably elevated in patients with heart failure (HF), being an independent predictor of mortality and heart transplantation (HT). However, its long-term prognostic role in patients undergoing a HT has not been investigated yet.

Methods: We retrospectively studied all patients who underwent a HT in our Advanced HF Unit, and had a previous determination of Ca125, since 2003 until 2012. Decompensated patients at the moment of the blood extraction and those whose survival was less than 1 month after HT were excluded. Pre-HT clinical, haemodynamical and follow-up data was analyzed.

Results: Of 173 patients who underwent a HT, 64 could be included in our study. When divided this population into normal or elevated Ca125 levels (>35U/mL, n=29), no significant differences were found according to their Baseline Characteristics. Survival was significantly inferior in the “Elevated Ca125” group (94 vs. 91%, 86 vs. 61 and 67 vs. 31% at 1, 3, 5 and 7 years, respectively, p<0.03) (Figure 1). Furthermore, “Elevated Ca125” group presented a clearly negative tendency to graft rejection. There were no differences according to infections, tumours or graft vascular disease.

Conclusions: In our population, non-congestive patients with high levels of Ca125 had an inferior long-term survival after Heart Transplant than those with normal levels. A tendency to less rejection existed in this group, too.

P2062 | BEDSIDE
Increased pump speed improves the exercise capacity of heart failure patients receiving left ventricular assist device support


Introduction: Left Ventricular Assist Devices (LVADs) are an established treatment for advanced heart failure. Continuous flow LVADs improve survival, functional status and quality of life in selected patients. However exercise capacity remains below normal despite LVAD support. At present, patients treated with a continuous flow LVAD are maintained at fixed pump speed. We have previously shown that a reduction of pump speed at fixed pump speed. We have previously shown that a reduction of pump speed at fixed pump speed would be beneficial.

Methods: We studied 20 ambulatory heart failure patients (18 males, age 52±14 years) receiving support with a HeartWare HVAD (n=14) or Thoratec HeartMate II (n=6). Indication for LVAD implantation was advanced heart failure (9 non-ischaemic DCM, 7 ischaemic DCM, 4 familial DCM, 18 male, age 52±14) with a bridge to transplantation strategy. Each patient underwent two treadmill exercise test, the first at their clinical pump speed (speed-fixed) and the other at increased pump speed (speed-inc). Clinical pump speed for HeartWare HVAD was 2844±200 rpm and for Thoratec HeartMate II was 9233±233 rpm. To minimise the risk of left ventricular suction events, the pump speed was increased prior to exercise under echocardiographic control and we aimed to temporarily increase pump speed between 10 to 15%.

Results: Overall, the second test was done at a 13% faster LVAD speed than the first. All cardiopulmonary exercise tests (n=40) were adequate and the peak respiratory exchange ratio (RER) was similar in both test (speed-fixed RER=1.17±0.12 versus speed-inc RER=1.16±0.11, p=0.59). Peak oxygen uptake (pkVO2) at speed-fixed was 15.5±3.4 mL/kg/min and increased to 16.6±3.6 mL/kg/min at speed-inc (p=0.001). This was associated with an increase in the estimated LVAD flow at peak exercise from 7.0±1.3 l/min during speed-fixed test to 8.1±1.0 l/min at speed-inc test (p=0.0014). The ventilatory efficiency during exercise remained unchanged (speed-fixed VE/VCO2 slope= 35.9±8.2 versus speed-inc VE/VCO2 slope= 35.2±7.3, p=0.30).

Conclusion: It was feasible to temporarily increase LVAD speed to increase aerobic exercise capacity and this resulted in a significant increase in peak oxygen consumption. Further studies are warranted to determine whether this phenomenon can be used to improve the exercise capacity of LVAD recipient.

P2063 | BEDSIDE
Effects of increasing donor age on the risk of permanent pacing after orthotopic heart transplantation

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Purpose: Due to extreme scarcity of donor hearts, increasingly older and marginal donor hearts are accepted for orthotopic heart transplantation (HTx). We evaluated the relationship between the donor age and the need for pacemaker (PM) implantation early or late after HTx.

Methods: Data of all consecutive patients transplanted between 1984 until 2014 at our centre were analysed (n=612, 74% male; median follow up of 97 months [IQR 38-150]). Three groups were created based on donor age: Group I (0–35 years, n=345), Group II (35–50 y, n=190) and Group III (>50 y, n=77). The primary outcome was permanent PM implantation after HTx for either sinus node dysfunction (SND) or AV block (AVD). The need for early (<90 days after HTx) or late PM (<90 days) was evaluated. The following secondary parameters were analysed: recipient age, ischaemic time and death.

Results: The mean recipient age at HTx was 46.4±14.3 years [range 2–72 y] and donor age 32.6±13.7 y. Significant older donor hearts were transplanted during the last ten years compared to the first ten years (40.1±15.9 y vs. 25.7±8.3 y, p<0.001) and more early PMs were implanted (10.2% vs. 1.7%, p<0.001). Ischaemic time (176±45 min vs. 181±48 min vs. 186±48 min, p<ns, respectively) was comparable for group I, II and III. Overall 11.3% (SND, n=31; AVB, n=38) received a PM after a median period of 10.6 months [IQR 1.3–94 months]. In group III a higher amount of early PM were implanted (11.7% vs. 9%) compared to group I (2.0%, p<0.001). For late PM implant equal rates were observed (6.5% vs. 6.4%, p<ns, respectively). In total 55% (n=342) died during follow up. The 10-year survival rate was 61%.

Conclusions: Increasing donor age, particularly >50 years, is a major risk factor for the need of permanent pacing post-HTx.

P2064 | BEDSIDE
Outcome of heart transplantation in the urgent receptor: whom should we choose?


Objectives: The improvement in the medical treatment of heart failure has allowed extending the survival of patients and delaying their entry in transplant’s list. Therefore, we receive receptors in worse clinical status with the need for urgent transplantation. We propose to compare the immediate and long-term results of heart transplant in patients with different levels of urgency.

Methods: From November 2003 to December 2012, 228 patients were submitted to cardiac transplantation. Pediatric patients and those in cardiogenic shock (with circulatory and/or ventilatory support) were excluded. From these, 58 (27%) were hospitalized and inotropic dependent [Group A] vs 154 (73%) who were waiting for transplant at home [Group B]. Patients in group A were younger (52.0±11.3 vs 55.2±10.4; P=0.050) and waited less for transplant (29.4±43.8 vs 48.8±45.2 days; P=0.006). No difference was found in gender (male sex: 77.6% vs 77.9%) or other comorbidities. Hemoglobin was lower in group A (12.2±2.2 vs 13.2±1.9; P=0.001) and bilirubin (1.5±0.1 vs 1.1±0.7; P=0.014) and creatinine (1.6±1.2 vs 1.4±0.4; P=0.010) were higher. Donor characteristics, such as age, sex, sex mismatch, inotropic and ventilatory support and cause of death were similar between groups. Mean follow-up time was 4.5±2.7 years.

Results: No difference was found in ischaemic (89.1±37.0 vs 91.5±34.5;
Purpose: In the era of improved survival and outcomes with continuous-flow left ventricular assist devices (CF-L VADs) as bridge to transplant (BTT), we sought to evaluate if our criteria for an acceptable donor heart have become more stringent. Materials and methods: We retrospectively reviewed all the donor offers at our institution from October 2011 to September 2012. Results: A total of 426 donor offers were reviewed: 81% (n=344) were declined and 19% (n=82) were accepted for heart transplantation. Of the declined offers, the most common causes of donor death included stroke (42%, n=44), anoxia (29%, n=102) and head trauma (23%, n=79). Ejection fraction (EF) was the strongest predictor of declining the offer, with every 1% decrease in EF increasing the odds of declining the donor heart by 6%. Older age, valvular abnormalities and IV drug use were also predictors of declining the donor offer. Death due to stroke almost doubled the odds of declining of the donor heart compared to anoxia, head trauma or other causes. Elevated creatinine had a marginally significant association with probability of declining the donor offer (Table 1).

<table>
<thead>
<tr>
<th>Donor Heart Information</th>
<th>Odds ratio</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.02</td>
<td>(1.001, 1.04)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anoxia</td>
<td>0.48</td>
<td>(0.221, 1.02)</td>
<td>0.09</td>
</tr>
<tr>
<td>CVA/stroke</td>
<td>ref</td>
<td>(ref)</td>
<td></td>
</tr>
<tr>
<td>Head trauma</td>
<td>0.41</td>
<td>(0.200, 0.84)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0.51</td>
<td>(0.151, 1.97)</td>
<td></td>
</tr>
<tr>
<td>IV drug use</td>
<td>5.17</td>
<td>(1.423, 18.58)</td>
<td>0.01</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>0.94</td>
<td>(0.910, 0.97)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Valve abnormalities</td>
<td>1.93</td>
<td>(1.073, 3.58)</td>
<td>0.03</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.20</td>
<td>(0.961, 1.50)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Odds of donor offer decline. Multivariable logistic regression analysis.

Conclusion: Donor death by stroke, decreased EF, older age, valvular abnormalities and IV drug use were identified as predictors of declining the heart for transplantation. The high percentage of declined offers reflects the quality of donor offers as opposed to change in our acceptance criteria. These data may have important implications in the current era of improved survival with CF-LVADs as BTT.

P2067 | BEDSIDE

Performance of five different bleeding-prediction scores in patients with acute pulmonary embolism

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Purpose: Bleeding-prediction scores may help guiding therapeutic management of patients with acute pulmonary embolism (PE), although no such score has been validated for this patient category. We aimed to externally validate and compare two risk bleeding-scores for venous thromboembolism (VTE) with three risk scores developed for patients with atrial fibrillation in a “real-world” cohort of consecutive PE patients.

Methods: We performed a prospective observational cohort study in 425 patients with acute PE who were treated with heparins followed by vitamin-K-antagonists. The Kuijer score, RIETE score, HEMORR2HAGES, HASBLED, and A TRIA were assessed at baseline. All patients were followed for the occurrence of major bleeding over a 30-day period, and over a 6-month period in a consecutive subsample of 129 patients. The accuracies of the original 3-level and newly defined 2-level outcome of the scores were compared.

Results: Overall, 25 of 425 (cumulative incidence 5.9% [95%CI 3.7-8.1%]) patients suffered a major bleeding within 30 days, with a case fatality rate of 8.0% (95%CI 1.1-26). The 6-month cumulative bleeding-incidence was 8.6% (95%CI 2.5–17%) with a case fatality rate of 0.0%. The predictive power of all five bleeding-scores was poor, with c-statistics ranging between 0.45 and 0.63 (Figure). Results were comparable for the 3-level and 2-level score outcomes, and for both follow-up periods. No individual score was found to be superior.

NEW INSIGHTS IN ACUTE PULMONARY EMBOLISM

P2068 | BEDSIDE

Non-pharmacological issues in advanced heart failure / New insights in acute pulmonary embolism

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Purpose: Endomyocardial biopsy (EMB) is routinely performed to monitor acute cellular rejection after cardiac transplantation. However, EMB is an invasive procedure that carries a risk of adverse effects and complications. The aim of this study was to evaluate the incidence of acute rejection episodes within the first year after transplantation in surveillance EMBs, and to evaluate a risk/benefit ratio of surveillance EMBs according to rejection rate requiring treatment to complications rate.

Methods: A total of 333 adult patients after cardiac transplantation undergoing 12 surveillance endomyocardial biopsies at predefined timepoints within the first year after transplantation were studied. During this time a total of 3401 endomyocardial biopsies were performed. 3328 (97.8%) were surveillance EMBs. EMBs due to clinical suspicion for acute rejection or control after biopsy proven acute rejection (n=73, 2.2%) were excluded from the study. Complications were defined as: presence of hemopericardium requiring drainage, hematoma from puncture site, pneumothorax, vascular injury and non representative endomyocardial biopsy. The benefit ratio was calculated considering the incidence of acute rejection with the complication rate.

Results: During the first 2 weeks after HTX 643 EMBs revealed 6 rejection episodes (0.9%), 19 complications (2.9%) occurred resulting in a benefit ratio of 0.31. Three weeks after HTX 308 biopsies revealed 17 rejections (5.5%), 13 complications (4.2%) resulted in a benefit ratio of 1.3. After four weeks 303 biopsies detected 8 rejections (2.6%), 15 complications (4.9%), benefit ratio: 0.53. During five week to twelve the 5th to 7th EMBs were performed with a total of 733 biopsies revealing 22 rejections (3.0%), 30 complications (4.1%) resulted in a benefit ratio of 0.73. After that 1340 biopsies (8th to 12th EMB) detected 22 rejections (1.6%), 24 complications (1.8%) resulted in a benefit ratio of 0.88.

Conclusions: Three weeks after cardiac transplantation there is a peak of rejection. It is the only timepoint, when the risk of rejection is higher than the procedural risk of EMB resulting in a positive benefit ratio. Our data show that surveillance biopsy in the 3rd week makes sense whereas other EMBs should be performed on clinical suspicion rather than scheduled surveillance biopsies. In a modern era of immunosuppression rigid biopsy regimens should be reconsidered and further development of rejection surveillance is warranted.
P2068 | BEDSIDE
Optimized high sensitive troponin T cut-off values for risk stratification of normotensive patients with pulmonary embolism
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Purpose: High sensitive troponin T (hsTnT) values ≤14 pg/ml help identify normotensive pulmonary embolism (PE) patients at low-risk. Whether optimized cut-off values for hsTnT and adjustment for age provides superior information for identification of intermediate-risk patients is unknown.

Methods: The prospective study studied 662 consecutive patients with acute PE from 13 participating European centres (median age, 70 [54-78] years). hsTnT was measured on admission using a highly sensitive quantitative electrochemiluminescence immunoassay.

Results: Overall, 29 patients (4.3%) had an adverse 30-day outcome (PE-related death, need for CPR, catecholamines, or intubation). The calculated optimal hsTnT cut-off value of 33 pg/ml (AUC, 0.74 [0.67-0.82], p < 0.001) was associated with a 6.32-fold increased risk of an adverse outcome (2.55-15.87, p < 0.001) which was inferior compared to the prognostic information provided by the established simplified Pulmonary Embolism Severity Index (sPESI; p = 0.002). Although hsTnT concentrations correlated with age (r=0.317; p < 0.001) and GRFR (r=0.314, p < 0.001), in multivariable analysis the prognostic value of hsTnT >14 pg/ml was independent from age and renal insufficiency (OR, 7.79 [1.60-33.30], p = 0.006). Moreover, hsTnT levels on admission or its prognostic value were not affected by the duration of symptoms prior to admission. While age-adjusted hsTnT cut-off values (<65 years, 25 pg/ml; 65-79.9 years, 35 pg/ml; ≥80 years, 45 pg/ml) did not provide additive information in patients >80 years, hsTnT was of prognostic value in patients >80 only if the age-adjusted cut-off value was used (OR, 6.23 [2.62-14.81], p < 0.001). A two-step approach based on the sPESI in the first step, and either hsTnT >14 pg/ml in patients sPESI ≥1 points or RV dysfunction on echocardiography in patients with sPESI ≥1 point(s) as a second step was developed. This simple strategy identified an ‘intermediate risk’ population with a 11.5% risk of an adverse outcome (n=156 [22.9%], sPESI ≥1 point(s) and RV dysfunction), and a ‘very low risk’ population with a 0% rate of adverse events (n=156 [22.9%], sPESI ≤1 point(s) and sTnT ≤14 pg/ml).

Conclusion: Although troponin levels were assumed to be affected by renal function, age, and symptom duration, in the present study optimized cut-off values for hsTnT and adjustment for age provided superior information for identification of intermediate-risk patients with acute PE as compared to the simplified PESI.

P2069 | BEDSIDE
Combination with clinical parameters optimises the prognostic value of heart-type fatty acid-binding protein (H-FABP) in normotensive patients with pulmonary embolism
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Purpose: Recent evidence derived from single-centre cohort studies suggests that heart-type fatty acid-binding protein (H-FABP) may reliably predict an adverse outcome of patients with pulmonary embolism (PE) with and without deep-vein thrombosis (DVT). Moreover, we sought to test the hypothesis that H-FABP cut-off values could be optimized if H-FABP was combined with clinical information based on the simplified Pulmonary Embolism Severity Index (sPESI). This study evaluates the predictive value of H-FABP in a large prospective, multicentre cohort of normotensive patients with acute PE. An adverse outcome was defined as death from any cause or haemodynamic collapse (systolic blood pressure <90 mmHg for at least 15 minutes, need for catecholamine administration, endotracheal intubation, or cardiopulmonary resuscitation) within the first 30-days. H-FABP was determined using an immunoturbidimetric assay.

Results: The study included 716 haemodynamically stable patients with acute symptomatic PE. During the 30-day study period, 41 patients (5.7%) had an adverse outcome. These patients had significantly higher baseline H-FABP values (median 3.1 [1.1-14.4] ng/ml) compared to patients with a favourable outcome (4.1 [2.5 to 6.5] ng/ml; p < 0.006). Overall, 209 patients (29.2%) had H-FABP levels above the predefined cut-off value of 6 ng/ml; of those, 19 patients (9.1%) had an adverse 30-day outcome compared to 22 (4.3%) of those with H-FABP levels ≤6 ng/ml (sensitivity, 46%; specificity, 72%; positive predicive value [PPV] 9%; negative predictive value [NPV] 96%; p < 0.001). Using logistic regression, H-FABP >6 ng/ml was associated with a 2.2-fold increase in risk of an adverse outcome (95% CI, 1.17 to 4.17; p = 0.015).

P2070 | BEDSIDE
Thrombolytic therapy in hemodynamically stable patients with acutepulmonary embolism: a meta-analysis
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Purpose: The role of thrombolysis in hemodynamically stable patients with acute pulmonary embolism (PE) remains a matter of debate. We performed a meta-analysis of randomized trials to assess the efficacy and safety of thrombolysis in these patients.

Methods: We searched in MEDLINE and EMBASE for randomized studies comparing thrombolysis and heparin for the initial treatment of PE in hemodynamically stable patients. The primary outcome of the study was overall death occurring during hospital stay or up to 30 days from acute PE. Secondary outcomes were major bleeding (MB), intracranial hemorrhage (ICH), mortality, and pulmonary embolism during hospital stay or up to 30 days from acute PE. We measured death, need for CPR, catecholamines, or intubation). The calculated optimal cut-off values for hsTnT and adjustment for age provided superior information for identification of intermediate-risk patients as compared to the simplified PESI.

Results: Ten studies were included in the meta-analysis (1761 patients), six with rt-PA, three with tenecteplase and one with urokinase. A not significant risk reduction for overall death in favor of thrombolysis compared with heparin was found (1.8% vs 2.3% in 1500 patients, OR 0.86, 95% CI 0.45 to 1.65, P = 0.35). Patients randomized to receive thrombolytic agents had an increased risk of major bleeding for MB (5.9% vs 1.9%; OR 2.87, 95% CI 1.68 to 4.90, P = 0.001) and for ICH (1.76% versus 0.57%; OR 2.47, 95% CI 1.00 to 6.14, P = 0.02), and a not significant increased risk for fatal bleeding (0.8% versus 0.4%; OR 1.95, 95% CI 0.53 to 4.19. P = 0.08). A not significant reduction in recurrent PE was found in favor of thrombolysis (9 studies, 1748 patients; 1.14% vs 2.28%; OR 0.5, 95% CI 0.23 to 1.07, P = 0.9). NNT to avoid one death was 334 patients. NNH to cause a MB or ICH were also calculated.

Conclusions: The risk for major bleeding and ICH in hemodynamically stable PE patients with PE is substantial with thrombolysis without evidence of a mortality benefit. This imbalance was higher in patients receiving tenecteplase.
history of PE and DVT (p<0.001) after 8.2±4.3 months without anticoagulation (p<0.05 for the time), including 3 (5.4%) and 9 (20.9%) PE episodes, respectively (p<0.05). The patients with PE who experienced recurrent VTE from both groups had more frequently unprovoked VTE, higher BMI, worse fibrin clot profile and higher plasma D-dimer compared with those free of recurrences during follow-up.

Conclusions: Altered fibrin clot features differ between patients with isolated PE and those with concomitant DVT. More prothrombotic profile of plasma fibrin variables, including denser fibrin networks and more efficient clot lysis, can help identify patients at increased risk of recurrent VTE. The study provides the first evidence for a potential role of clot phenotype after cessation of anticoagulation in predicting recurrence of VTE in patients with previous PE.

P2072 | BEDSIDE
Meta-analysis of impending paradoxical embolism
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Purpose: Impending paradoxical embolism (IPDE) occurs when thrombus is entrapped within a patent foramen ovale (PFO), most frequently occurring in the setting of acute pulmonary embolism. We aimed to review all reported cases of IPDE, compare survival with each treatment method and identify patient characteristics within each group.

Methods: Systematic electronic literature searches using a pre-defined search strategy identified 239 patients for inclusion in the review. Disease, demographic, treatment and outcome data was collected for analysis. Authors of manuscripts were contacted if information was incomplete. Non-english language studies were translated for inclusion.

Results: 239 case reports were included for review. There were 110 males and 129 females and the average age was 58 years. Common presenting symptoms were dyspnoea (74%), chest pain (28%), stroke/TIA (26%) and syncope/presyncope (23%). Most patients (82%) had pulmonary embolism confirmed by imaging. 73 patients (30%) experienced systemic embolism prior to diagnosis of IPDE. IPDE was diagnosed most frequently using transthoracic and transoesophageal echocardiography. Reported treatments included emergency surgery, thrombolysis and anticoagulation. Mortality at discharge was 15% in the surgery group, 18% in the anticoagulation group and 28% in the thrombolysis group (p=0.016). There was some evidence that male sex and patients presenting with cardiac arrest, hypotension and haemoptysis were more likely to be deceased at hospital discharge. In adjusted multivariate analysis, treatment modality was not significantly associated with mortality at discharge.

Conclusions: This is the largest review of IPDE to date and attempts to provide clinicians with information regarding the diagnosis and management of this infrequent reported condition. The absence of prospective studies limits the conclusions that can be drawn from this review. Reported mortality at discharge was lower in the surgery and anticoagulation groups, however this difference was not significant in multivariate modelling.

P2073 | BEDSIDE
Use of a diagnostic computerized decision support system and outcomes of suspected pulmonary embolism
D. Jimenez1, C. Jurkovic1, A.K. Portillo1, V. Gomez1, J. Corres1, A. Vicente1, P. Den Exter2, M.V. Huisman2, L. Moores3, R.D. Yusen4, 1University Hospital Ramon y Cajal, Madrid, Spain; 2Leiden University Medical Center, Leiden, Netherlands; 3Edward Hebert School of Medicine, Bethesda, United States of America; 4Washington University School of Medicine, St. Louis, United States of America

Background: The diagnostic approach to patients with suspected acute pulmonary embolism (PE) evaluated in an Emergency Department (ED) may affect test utilization, test yield, and patient outcomes.

Methods: This single center cohort study aimed to determine the effects of evidence-based clinical decision support (CDS) on the use of computed tomographic pulmonary angiography (CTPA) (number of patients undergoing CTPA per 1000 ED visits), the yield (percentage of patients with CTPA positive for acute PE), and outcomes of patients with negative diagnostic work-up for PE. The study included patients with suspected PE before the postdischarge period (from January 1, 2011 to December 31, 2011) and prospectively after (postdischarge period) (from January 1, 2012 to December 31, 2012) the introduction of CDS. Investigators assessed patients with negative diagnostic work-up for symptomatic venous thromboembolic events that occurred during 3-months of follow-up.

Findings: The study analyzed 652 patients preintervention and 711 patients postintervention (total 1,363). A greater proportion of patients received CTPA testing in the postintervention period than in the postdischarge period (55% vs. 49%; absolute difference [AD] = 6.3%; 95% CI, 1.0% to 11.6%; P = 0.02). CTPA use increased preintervention (21.5% increase, from 2,60 to 3.16 examinations per 1000 patients; P = 0.17) and decreased postintervention (25.4% decrease, from 3.16 to 2.38 examinations per 1000 patients; P = 0.06). Of the 302 CTPA examinations performed during the postintervention period, 112 (31%) were positive for PE. Of the 350 CTPA examinations performed during the postintervention period, 116 (33%) were positive for PE. Yield increased from 26.0% to 46.5% (P = 0.01) postintervention. Of the patients with a negative diagnostic work-up for PE, the frequency of possible and definite venous thromboembolic events was low (20 of 1,065 patients; 1.9%; 95% confidence interval [CI], 1.1% to 2.7%) during follow-up. Sixteen events (16 of 492 patients; 3.2%; 95% CI, 1.7% to 4.8%) occurred in the preintervention group, whereas 4 events (4 of 573 patients; 0.7%; 95% CI, 0.0% to 1.4%) occurred in the postintervention group (AD, 2.5%; 95% CI, 0.9% to 4.6%; P = 0.01).

Interpretation: Implementation of evidence-based CDS in the ED for patients with suspected PE associated with a decrease in CTPA use, an increase in postdischarge period, and a small but significant decrease in possible and definite thromboembolic events in patients that had a negative initial diagnostic work-up for PE.
the derivation and validation cohorts. The c statistics among treatment subgroups were 0.72, 0.79 and 0.80 for oral anticoagulation, dual and single antiplatelet therapy, respectively. In a time-updated covariate-adj usted Cox proportional hazards regression model, 1-year bleeding was an independent predictor of mortality. Conclusion: The CardioChUS bleeding score quantifies risk for 1-year major bleeding across all postdischarge antithrombotic treatments, which enhances bleeding risk assessment for post-discharge selection of antithrombotic treatments and the development of strategies to mitigate that risk.

P2076 | BEDSIDE
Continued high CVD risk in myocardial infarction survivors: comparison of risk first and second year after MI - results from a Swedish nationwide study
T. Jernberg1, H. Hjelm2, P. Hasvold3, M. Henriksen4, M. Thurer4, M. Janzon5. 1Karolinska Institute, Dept of Medicine, Huddinge, Stockholm, Sweden; 2Dept of Medicine, Nyköping, Sweden; 3Astra Zeneca, Södertälje, Sweden; 4Statistiken, Uppsala, Sweden; 5Linköping University Hospital, Linköping, Sweden

Background: Although short-term survival after myocardial infarction (MI) is improving, the long-term risks of cardiovascular disease (CVD) in a clinical practice setting are not known. The aim of this study was to investigate the CVD risk during the first and second year post discharge after non-fatal MI using nationwide registry data.

Method: All patients surviving an MI in Sweden between July 1, 2006 and June 30, 2011 were identified and followed in the compulsory nationwide patient registry which includes all discharge diagnoses. These data were also linked to the cause of death register. The primary endpoint consisted of MI, stroke and CVD mortality. Hazard ratios (HR) adjusted for gender, age, stroke, MI, diabetes and heart failure (HF) are reported.

Results: A total of 97,254 patients (median age 74 years) with 2.7 years median follow up covering 277,118 patient-years were included. Age (60-69 vs <60: HR [95% CI]: 1.37 [1.30-1.44], 70-79 vs <60: 2.18 [2.08-2.29], 80+ vs <60: 4.59 [4.38-4.81]), prior MI (1.46 [1.42-1.50]), stroke (1.59 [1.55-1.63]), diabetes (1.36 [1.33-1.39]) and HF (1.67 [1.63-1.71]) were all independently associated with higher risk of the primary endpoint in the first year. For patients without a non-fatal MI the first year, the overall risk remained high in the second year (11.3% compared with 18.3% in the first year), and the relative importance of each risk factor was similar to the first year (Figure).

Conclusions: Nationwide data for all non-fatal MI patients in Sweden show that the CVD risk remains high also in the second year post MI and that the relative importance of risk factors appears similar over time.

P2078 | BEDSIDE
Long-term mortality among young patients with acute myocardial infarction referenced against a background population
M.Y. Chan1, F. Gao2, M. Jing1, L. Simi2, T. Koh3, D. Foo4, H. Ong5, H. Tan1, T. Yeo1, T. Chua2 on behalf of Singapore Cardiac Databank. 1National University Heart Centre, Department of Cardiology, Singapore, Singapore; 2National Heart Centre Singapore, Singapore, Singapore; 3Tan Tock Seng Hospital, Singapore, Singapore; 4Khoo Teck Puat Hospital, Singapore, Singapore

Background: Young patients with acute myocardial infarction (AMI) have a more favorable prognosis than older patients with AMI. However, there are limited data comparing the prognosis of young AMI patients with young population controls. Because of their increased resilience, the prognosis of young AMI patients may approximate that of age-matched community counterparts over time.

Methods: We studied 15,151 patients diagnosed with AMI from 2000-2005, of which 601 patients were <40 years of age (young). The relative mortality ratio was calculated as the ratio of the observed mortality of patients with AMI over the expected mortality estimated from the background Singapore population (n=317,7000) with similar sex, age and period characteristics. A relative mortality ratio of 1.0 or >1.0 indicates lower or greater mortality, respectively, than the background population.

Results: The 12-year all-cause and cardiovascular mortality of young vs. older patients was 12.8% vs 50.7% (P<0.001) and 9.2% vs. 34.5% (P<0.001) respectively. The adjusted hazard ratio of all-cause and cardiovascular mortality comparing young with older patients was 0.20 (0.16-0.27) and 0.27 (0.20-0.36) respectively. The relative mortality ratio (95% CI) of young vs. older patients at 1 year, 3 year, 5 year and 9 year was 1.03 (1.02-1.05) vs. 1.24 (1.23-1.25), 1.04 (1.03-1.07) vs. 1.33 (1.31-1.34), 1.06 (1.04-1.09) vs. 1.40 (1.38-1.41), and 1.10 (1.07-1.14) vs. 1.57 (1.53-1.61), respectively.

Conclusions: Despite a five-fold lower long-term mortality than older patients, young AMI patients remain at a significantly greater cumulative risk of long-term mortality than an age-matched background population. Better measures are needed to mitigate the long-term residual risk associated with young onset AMI.
P2079 | BEDSIDE
Serum uric acid is associated with mortality and heart failure hospitalizations in patients with complicated myocardial infarction: analysis from High Risk Myocardial Infarction Database Initiative
T.G. Von Lueder1, N. Giredo2, D. Atar1, S. Agevali1, Z. Larn1, K. Dickstein1, F. Zannad2, P. Rossignoli2 on behalf of the High Risk Myocardial Infarction Database Initiative. 1Oslo University Hospital, Department of Cardiology, Oslo, Norway; 2Clinical Investigation Centre Pierre Drouin (CIC-P), Nancy, France; 3Stavanger University Hospital, Stavanger, Norway

Background: Serum uric acid (SUA) levels predict poor outcome in patients with stable coronary heart disease. Whether SUA predicts outcome in acute myocardial infarction (MI) complicated by reduced left ventricular (LV) function, heart failure (HF) or both is unknown.

Methods: We studied the association between baseline SUA and outcomes using univariable and multivariable Cox models in an individual-patient data meta-analysis of 4 large randomized trials of high-risk MI (CAPRICORN, EPHEMUS, OPTIMAL and VALIANT; N=28,771).

Results: SUA was available in 12,677 patients (median follow-up 1.9 years). Patients were separated into quartiles (Q) according to baseline SUA (Q1, 45-280; Q2, 281-344; Q3, 345-420; Q4, 420-1640 micromol/l). Patients in higher SUA quartiles were older, more symptomatic, and had more comorbidity. Renal failure prevalence was 10-fold higher in Q4 vs Q1. All-cause survival at 3-years was 86.8% in Q1 vs 69.4% in Q4 (fig. A). Most deaths were due to CV disease (fig. B). In univariable analysis, all-cause mortality rose across SUA quartiles (Hazard ratio (HR)=1.06, confidence interval (CI)=0.92-1.22 for Q2; HR=1.57, CI=1.31-1.71 for Q3; HR=2.70, CI=2.35-3.10 for Q4 vs Q1) and HF hospitalization (HR=1.72, CI=1.61-1.84 for Q4 vs Q1). Multivariable analysis models adjusted for baseline characteristics consistently showed that SUA independently predicted all-cause mortality (HR=1.78, CI=1.51-2.09 for Q4 vs Q1), CV mortality (HR=2.70, CI=2.35-3.10 for Q4 vs Q1) and HF hospitalization. Analysis in patients without diuretics yielded similar results.

Conclusions: Elevated SUA was a strong and independent predictor of poor clinical outcomes in patients after acute high-risk MI complicated by reduced LV function, HF or both.

P2080 | BEDSIDE
Long-term follow-up after intraconary infusion of mononuclear cells from bone marrow or peripheral blood after acute myocardial infarction: 5 year results of the randomized controlled HEBE trial
R. Delewi1, A.M. Van Der Laan1, L. Robbers2, A. Hirsch1, R. Nijveldt2, J.G.P. Tijssen1, R.A. Tio3, A.C. Van Rossum2, J.J. Piek1, F. Zijlstra4 on behalf of the HEBE study investigators. 1Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; 2VU University Medical Center, Amsterdam, Netherlands; 3University Medical Center Groningen, Groningen, Netherlands; 4Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands

Objectives: There is limited data on the long-term outcomes of intraconary transplantation of bone marrow mononuclear cells (BMMCs) and peripheral blood mononuclear cells (PBMCs) for the treatment of acute myocardial infarction patients; the results of the randomized controlled HEBE study.

Methods: The HEBE study is a multicenter trial that randomized 200 patients with large first AMI treated with primary percutaneous coronary intervention (PCI) to either intraconary infusion of BMMCs (n=69), PBMCs (n=66), or standard therapy (n=65). Patients were followed for 5 years after AMI to assess clinical adverse events, including death, myocardial reinfarction and hospitalisation for heart failure.

Results: During five years of follow-up, six patients assigned to the PBMC group died, compared to two patients in the control group (p=0.27). Ten patients treated with PBMC therapy had a recurrent myocardial infarction, compared to one in the control group (p=0.009). The composite endpoint of death, recurrent myocardial infarction was significantly higher in the PBMC group compared to controls (14 patients versus 3 patients, p=0.008). Improvement of left ventricular ejection fraction (LVEF) during follow-up was 4.2±8.6% in the BMMC group and 3.0±8.3% in the PBMC group, compared to 4.0±6.8% in the control group (p=0.37 and p=0.17, respectively).

Conclusion: Term follow-up of the HEBE trial showed no beneficial effect of intracoronary delivery of mononuclear cells from bone marrow or peripheral blood on regional and global systolic myocardial function at follow-up. However, major clinical cardiovascular adverse events were significantly higher in the PBMC group.

VALVE SURGERY: FROM PREDICTION TO OUTCOME
P2081 | BEDSIDE
Graft sizing in David reimplantation technique using echocardiographic based formulas
M.V. Regel, M.I.M. Versteeg, R.J.M. Klautz, M.J. Schalj, J.J. Bax, N. Ajmone Marsan, V. Delgado, Heart Center Leiden, Leiden, Netherlands

Purpose: It remains unclear whether a transthoracic echocardiography (TTE)-based formula may help in selecting the graft size during David reimplantation technique for aortic root dilatation.

Methods: Forty-nine patients (47±11 years old, 84% men) who underwent David reimplantation technique were evaluated. Leaflet height and leaflet area TTE-based formulas were developed to select the graft size (Figure 1). The implanted graft size was based on the David’s formula (diameter=2·2/3(leaflet height+2)), measuring the leaflet height with surgical calipers. The agreement between these formulas and the eventually implanted graft size was evaluated in 26 patients who underwent isolated David reimplantation without additional leaflet repair. In addition, the incidence of mild residual aortic regurgitation (AR) for each formula was evaluated.

Results: The incidence of mild residual AR was 24% in all patients. The implanted grafts were divided into quartiles and were compared to the TTE-based formulas. The Kappa measure of agreement between the implanted graft size and calculated size using the leaflet height and leaflet area TTE-based formulas was 0.335 (p=0.002) and 0.366 (p<0.001), respectively. In patients who received the same or smaller graft than calculated using the leaflet height and leaflet area TTE-based formulas, the incidence of mild AR was 10% and 8%, respectively, whereas in patients who received a larger graft than calculated, the incidence of mild AR was 38% and 46%, respectively (p=0.124 and p=0.027, respectively).

Conclusion: In patients undergoing David reimplantation technique, graft sizing can be performed with TTE. The incidence of mild residual AR was lower when the implanted graft was similar or smaller than calculated compared to a larger implanted graft than calculated.
Results: 200 patients [83±3 years, 53% men, EuroSCORE II and II, 10.1 (7.9-17.2) and 3.6 (2.6-5.5), respectively. The surgeries were: CABB (35.9%), Isolated Valve surgery (41.1%) and CABB + Valve (22.9%). Selected outcomes were: reoperation (5.2%), major complications (12.5%), hospital mortality (12.0%), EuroSCORE II was higher in the CABB group than in the CABB + Valve group, while valve isolates were (6.3% vs 4.2%, p=0.03). In multivariate analysis, independent predictors of mortality were only LVEF (OR = 1.1, 95 CI 1.01-1.11) and COPD (OR = 5.1, 95 CI 1.21-21). For clinical performance of the ES II in different surgical groups, the O/E ratio was: Global (2.53), CRM (2.76), valve (3.18) and valve (3.36), p<0.05 for all values. The calculation for groups of low, moderate, high and very high risk was respectively 0, 2.88, 2.50, and 2.6 (Hosmer - Lemeshow test p=0.01). The accuracy of the EuroSCORE II was slightly superior to the EuroSCORE I, although both have shown in discrimination (ROC AUC 0.82 and 0.84, respectively p<0.05). ES II appropriately reclassified the risk in relation to ES I, in only 7.3% of patients (NRI for events: 65.2%; NRI for non events: 57.9%).

Conclusions: In octogenarians, the ES II was not an independent predictor of death, underestimated the surgical risk, had low discrimination (although higher than the ES I) and poor calibration in the different risk categories. It appropriately reclassified only 7% of patients, compared to the ES I. New specific risk scores to this age group should be developed and validated to enable adequate stratification of cardiac surgical risk.

P2087 | BEDSIDE
Incidence and clinical impact of homograft stenosis in long term follow up after Ross intervention
M. Ruiz Ortíz1, M. Delgado1, D. Mesa1, R. Villalba2, L. Pardo1, F. Hidalgo1, S. Rodriguez Diego1, P. Alados3, J. Casares4, J. Suarez De Lezo5, 1Cardiology Department, University Hospital Reina Sofia, Cordoba, Spain; 2Regional Blood Transfusion Center and Tissue Establishment, Cordoba, Spain; 3Cardiovascular Surgery Department. University Hospital Reina Sofia, Cordoba, Spain

Purpose: Ross intervention is an alternative to mechanical prostheses implantation in young and middle-aged patients that need aortic valve surgery. Despite the absence of homograft stenosis and the need of homograft reintervention are possible complications in these patients. Our aim was to describe the incidence and the clinical impact of this complication in a prospective series of a reference cardiovascular surgery hospital, during a median follow up of three years. Each patient had undergone the following investigations: 24-hour blood pressure (BP) monitoring, biological assays, carotid-to-femoral pulse wave velocity and polysomnography. The prevalence of OSA and uncontrolled hypertension were high (89%, and 77% respectively). Forty two patients (67%) presented no AAE. Mean nocturnal oxygen saturation ($SpO_2$) was significantly lower in patients with AAE than in those without AAE (92.5± 1.9 vs. 93.6± 1.7, p<0.04). In patients who recorded progression in aortic diameter, the VmaxAo was significantly correlated to the 24-hour SBP (r=0.273, p<0.013) and mean nocturnal $SpO_2$ (r=0.381, p=0.002). In multivariate analysis, $SpO_2$ was independently and positively correlated to mean nocturnal progression ($SpO_2$). Logistic regression modeling showed that mean nocturnal $SpO_2$ was independently associated with AAE (OR=4.36, 95% CI 1.34-14.04, p<0.01).

Conclusions: This study shows a high prevalence of OSA in patients after surgery for AAS. Moreover, severe nocturnal hypoxemia was significantly related to a more rapid AAE. These findings prompt a systematic search and treatment of OSA during patient follow-up.
available in 91 patients (85%) and clinical data in 104 patients (98%). 26/91 patients (29%) developed at least moderate homograft stenosis (peak echocardiographic gradient ≥ 36 mmHg) and 10/104 patients (9.6%) underwent 13 procedures over the homograft: in 3 patients, the homograft was substituted surgically. 3 patients underwent a percutaneous pulmonary valve implantation and one patient needed a stent implantation. The other 3 patients underwent 2 procedures: a stent implantation and, years later, a percutaneous pulmonary valve implantation; a percutaneous pulmonary valve implantation and a surgical intervention years later; and finally, a pulmonary valvuloplasty and years later, a percutaneous pulmonary valve implantation. This patient died because of an acute myocardial infarction as a complication of the last procedure. Survival free from homograft stenosis and homograft intervention was 96%, 82% and 75%, and 99%, 94% and 91% at 1, 5 and 10 years, respectively. Pediatric patients (<18 years) had a worse survival free from homograft stenosis (HR 0.95, 95%CI 0.56–7.90, p = 0.003), although there was no significant difference regarding homograft reintervention (HR 2.01, 95% CI 0.52–7.78, p = 0.31). Younger age of the homograft donor was also a predictor of stenosis (HR 0.97, 95% CI 0.94–0.99, p = 0.046). Conclusion: In this study, probabilities of homograft stenosis and reintervention at ten year after Ross operation were 25% and 9%, respectively, and only one patient had a reintervention related death. A younger donor and recipient age was associated with a higher rate of stenosis.

### CARDIO-RENAL INTERACTION

#### P2088 | SPOTLIGHT

The association between kidney function within the normal or mildly impaired range and incident cardiovascular disease - a population based study with over 10 million cardiovascular events - a population based study with over 10 million cardiovascular events.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Chronic kidney disease eGFR &lt; 60 mL/min 1.73m² (%)</th>
<th>eGFR ≥ 60 mL/min 1.73m² (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>1.00 (1.07–1.14)</td>
<td>0.0001</td>
<td>0.91 (0.84–0.98)</td>
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<td>Waist circumference (cm)</td>
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<td>SBP (mmHg)</td>
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<td>1.03 (1.01–1.04)</td>
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<tr>
<td>DBP (mmHg)</td>
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<td>0.0001</td>
<td>1.00 (1.00–1.00)</td>
</tr>
<tr>
<td>Smoking*</td>
<td>0.83 (0.60–1.15)</td>
<td>0.2536</td>
<td>0.76 (0.51–1.12)</td>
</tr>
<tr>
<td>HLD-cholesterol (mg/dl)</td>
<td>0.97 (0.96–0.99)</td>
<td>0.0001</td>
<td>0.95 (0.92–0.98)</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
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<td>1.00 (1.00–1.01)</td>
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<tr>
<td>Triglycerides (mg/dl)</td>
<td>1.00 (1.00–1.00)</td>
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<td>1.00 (0.99–1.00)</td>
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<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>1.00 (1.00–1.00)</td>
<td>0.0001</td>
<td>1.00 (1.00–1.01)</td>
</tr>
<tr>
<td>White cell count (10³/μl)</td>
<td>0.71 (0.51–0.98)</td>
<td>0.0372</td>
<td>0.74 (0.71–0.76)</td>
</tr>
<tr>
<td>Clearing</td>
<td>0.92 (0.77–1.11)</td>
<td>0.3055</td>
<td>0.90 (0.74–1.07)</td>
</tr>
<tr>
<td>Odds ratios (OR), 95% confidence intervals (CI), expressed per unit of each variable.a Current consumption of at least one cigarette or pipe per day. b Drinkers (moderate/severe) vs non drinkers/occasional. c Chronic Kidney Disease - Epidemiology.</td>
<td></td>
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</tr>
</tbody>
</table>

#### P2089 | BEDSIDE

Study of associations between chronic kidney disease and cardiovascular and metabolic risk factors in the working population.

<table>
<thead>
<tr>
<th>Variable</th>
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<th>p-value</th>
<th>Adjusted OR (95% CI)</th>
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</thead>
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<tr>
<td>Age (years)</td>
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<td>0.0653</td>
<td>1.01 (1.00–1.02)</td>
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<tr>
<td>Gender</td>
<td>1.00 (0.99–1.01)</td>
<td>0.6188</td>
<td>1.00 (0.99–1.01)</td>
<td>0.6188</td>
</tr>
</tbody>
</table>

Conclusion: Our findings, derived from a large, population-based cohort, demonstrate that CKD is independently associated with a decrease of 2.3% and 0.9% in incident CVD, using CKD-EPI and MDRD, respectively (p < 0.001 for both). Using net reclassification analysis, stratifying patients to GFR deciles, CKD-EPI was more accurate in predicting incident CVD than MDR (Net Reclassification Index = 0.10, p < 0.001).

### P2090 | BENCH

Impact of chronic kidney disease on cardiovascular and metabolic risk factors, in the working population and the relevance of occult CKD.

Methods: Between 2010-2011, 61,106 workers (77.2% males, mean age 39.3 years, range 16 to 75), who underwent two consecutive yearly medical check-ups and had information for eGFR according to CKD-EPI equation (serum creatinine was measured by a IDS traceable method). CKD was defined by two eGFR < 60 ml/min.1.73m². Creatinine level within the normal range and with an abnormal eGFR was considered occult CKD.

Results: Multivariate analyses show that blood pressure and total cholesterol (positively) and HDL, LDL (negatively) were associated with CKD. Metabolic factors were associated (positively), 22% of women met the criteria for occult CKD (data not shown).

Logistic regression-associated factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Chronic kidney disease eGFR &lt; 60 mL/min 1.73m² (%)</th>
<th>eGFR ≥ 60 mL/min 1.73m² (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>1.10 (1.07–1.14)</td>
<td>0.0001</td>
<td>0.91 (0.84–0.98)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>1.05 (1.04–1.06)</td>
<td>0.0001</td>
<td>1.05 (1.03–1.08)</td>
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<td>SBP (mmHg)</td>
<td>1.04 (1.04–1.05)</td>
<td>0.0001</td>
<td>1.03 (1.01–1.04)</td>
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<td>DBP (mmHg)</td>
<td>1.00 (1.00–1.00)</td>
<td>0.0001</td>
<td>1.00 (1.00–1.00)</td>
</tr>
<tr>
<td>Smoking*</td>
<td>0.83 (0.60–1.15)</td>
<td>0.2536</td>
<td>0.76 (0.51–1.12)</td>
</tr>
<tr>
<td>HLD-cholesterol (mg/dl)</td>
<td>0.97 (0.96–0.99)</td>
<td>0.0001</td>
<td>0.95 (0.92–0.98)</td>
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<tr>
<td>LDL-cholesterol (mg/dl)</td>
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<td>0.0001</td>
<td>1.00 (1.00–1.01)</td>
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<tr>
<td>Triglycerides (mg/dl)</td>
<td>1.00 (1.00–1.00)</td>
<td>0.0001</td>
<td>1.00 (0.99–1.00)</td>
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<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>1.00 (1.00–1.00)</td>
<td>0.0001</td>
<td>1.00 (1.00–1.01)</td>
</tr>
<tr>
<td>White cell count (10³/μl)</td>
<td>0.71 (0.51–0.98)</td>
<td>0.0372</td>
<td>0.74 (0.71–0.76)</td>
</tr>
<tr>
<td>SD (Alcohol standard drink)*</td>
<td>0.92 (0.77–1.11)</td>
<td>0.3055</td>
<td>0.90 (0.74–1.07)</td>
</tr>
<tr>
<td>Odds ratios (OR), 95% confidence intervals (CI), expressed per unit of each variable.a Current consumption of at least one cigarette or pipe per day. b Drinkers (moderate/severe) vs non drinkers/occasional. c Chronic Kidney Disease - Epidemiology.</td>
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</table>

Conclusions: CKD was associated with an increased risk for cardiovascular and metabolic diseases that could be delayed by early detection and treatment, particularly by lowering blood pressure and other associated risk factors, included also at the occult stage.

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history of CHD on CV risk in high-risk hypertensive patients, as a subanalysis of CASE-J Ex.

Methods: The CASE-J trial compared the effects of the angiotensin II receptor blocker candesartan and the calcium channel blocker amlopidine on the incidence of CV events in 4,703 high-risk Japanese hypertensive patients. The CASE-J Ex- tension (CASE-J Ex) was an observational study designed to evaluate their long-term effects, incorporating an additional 3-year follow-up of the CASE-J trial. CKD was defined as estimated glomerular filtration rate < 60 ml/min/1.73m² or proteinuria at baseline. We divided them into four groups according to baseline characteristics (non-CKD without a history of CHD, non-CKD with a history of CHD, CKD without a history of CHD, and CKD with a history of CHD). The primary endpoint was CV events including sudden death, cerebrovascular, cardiac, renal, and vascular events. We used the multiple Cox regression analysis to estimate the hazard ratio (HR) and 95% confidential interval (CI) with adjustment for baseline characteristics (prior antihypertensive treatment, allocated drug, age, sex, body mass index, diabetes mellitus, a history of previous myocardial infarction, peripheral vascular disease, hyperlipidemia, smoking, systolic and diastolic blood pressure).

Results: Of 4,703 patients, 339 (7.2%) patients experienced CV events for a rate of 15.9 per 1,000 person-years during 4.5 ± 1.9 years of follow-up. CKD with a history of CHD most frequently experienced CV events among four groups (adjusted HR: 4.87; 95%CI: 3.22-7.36; P < 0.001). Both non-CKD and a history of CHD with a history of CHD had higher risk of CV events compared to non-CKD without a history of CHD (adjusted HR: 3.23; 95%CI: 2.12-4.92; P < 0.001, adjusted HR: 2.81; 95%CI: 2.12-3.73; P < 0.001, respectively).

Conclusion: The present study suggested that patients with CKD have CV risk equivalent to patients with a history of CHD in high-risk hypertensive patients.

P2091 | BEDSIDE

Statins and Cardiovascular Primary Prevention in Individuals with Normal Renal Function: A Meta-analysis

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Purpose: Multiple meta-analyses have been performed of lipid lowering therapies for cardiovascular primary prevention in the general population without consideration of renal function. We therefore aimed to perform a systematic review and meta-analysis of lipid lowering therapies for cardiovascular primary prevention in individuals with normal renal function (estimated glomerular filtration rate > 60ml/min).

Methods: We performed a systematic review of Medline using a pre-defined search criteria and without language restrictions. We also reviewed other sources including the Cochrane Central Register of Controlled Trials and recent meta-analyses in both the general population and chronic kidney disease. We then performed a meta-analysis of the eligible trials using a random effects model. Our pre-defined primary outcome was cardiovascular events and our pre-defined secondary outcomes were total mortality, coronary heart disease events and stroke.

Results: Five trials were identified, all trials providing analysis by renal function were post-hoc subgroup analyses of statins in the general population. All trials presented analysis using the Modification of Diet in Renal Disease formula for estimated glomerular filtration rate.

The pooled risk ratio for cardiovascular disease events was 0.72 (95% confidence interval CI) 0.63 to 0.83, p < 0.00001. For the secondary outcomes the risk ratios were 0.82 (95% CI 0.71 to 0.95, p = 0.008) for total mortality, 0.71 (95% CI 0.62 to 0.81, p < 0.00001) for coronary heart disease events and 0.67 (95% CI 0.40 to 1.14, p = 0.14) for stroke.

When compared to a meta-analysis using the whole trial data, there were trends in all groups towards overestimation of the benefit of statins when renal function was not considered. For cardiovascular events this overestimation was by 5% (p = 0.18) and for mortality 10% (p = 0.09).

Conclusions: Statins for primary prevention of cardiovascular disease in individuals with normal renal function are effective. However compared to general individuals with normal renal function are effective. However compared to general

P2094 | BEDSIDE

Clinical impact of serum uric acid on the incidence of atrial fibrillation in a population-based cohort study

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Purpose: Current evidence suggests that serum uric acid (UA) could be a marker of oxidative damage, a factor reported as a part of the mechanism of atrial fibrillation (AF). Previous report indicated that the association of UA with AF risk differed by race and gender. However, no prospective study has examined the association between higher UA and incident AF in Asians. We assessed the hypothesis that higher UA is associated with increased incident AF in a Japanese urban cohort.
Method: A total of 6,906 participants (aged 30-84 years; 47% men) without prior AF were followed for 12.8 years, who underwent standard lead-1 electrocardiograms and biochemical examinations at baseline in a population-based prospective cohort. AF was diagnosed when AF or atrial fibrillation was present on electrocardiograms during a biannual health examination or when AF was indicated as an antecedent event in the medical record. UA levels were categorized into quartiles. Cox proportional hazards ratios (HRs) and 95% confidence intervals (CIs) for incident AF were analyzed after adjustment of cardiovascular risk factors such as age, body mass index, hypertension, hypercholesterolemia, diabetes, smoking, alcohol, and estimated glomerular filtration rate.

Results: During the follow-up, we identified 244 cases of incident AF (166 in men and 78 in women) including 31 cases of paroxysmal AF. In men, compared with the lowest UA quartile (≤5.2 mg/dl group), the multivariable-adjusted HRs (95% CI) for AF were 1.12 (1.07 to 1.17; p=0.001) in the UA 5.2 to 5.9 mg/dl group, 1.03 (0.96 to 1.05; p=0.33) in the UA 6.0 to 6.7 mg/dl group, and 1.68 (1.09 to 2.61; p=0.02) in the highest UA quartile (≥6.7 mg/dl group). In women, compared with the lowest UA quartile (≤3.9 mg/dl group), the multivariable-adjusted HRs (95% CI) for incident AF were 0.67 (0.31 to 1.43; p=0.29) in the UA 3.9 to 4.4 mg/dl group, 0.70 (0.35 to 1.40; p=0.31) in the UA 4.5 to 5.1 mg/dl group, and 1.25 (0.65 to 2.37; p=0.005) in the highest UA quartile (>5.1 mg/dl group). Even after adjustment of cerebral and cardiovascular diseases, higher UA is associated with increased incident AF in men. Probabilities for trend were 0.03 and 0.37 in men and women, respectively.

Conclusion: The higher levels of UA were associated with an increased risk for incident AF in Japanese general population of men independent of confounding factors.

REGIONAL AND ETHNIC PROFILES

P2095 | BENCH
Clinic and ambulatory hypertension among high altitude dwellers. P2095 | BENCH

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Background: Arterial hypertension is highly prevalent among lowlanders, being a major risk factor for morbidity and disability worldwide. However, little is known about its prevalence and determinants in high altitude dwellers. Moreover, available information relies on casual office blood pressure (BP) measurements, while data obtained with ambulatory BP monitoring are lacking.

Methods: We performed ambulatory BP monitoring and collected basic clinical data obtained with ambulatory BP monitoring are lacking.

Results: Complete data were obtained in 286 subjects (age 38.2±13.1 years, 143M/143F, BMI 25.3±3.4 kg/m², SBP 138±4.4 mmHg, diastolic BP (DBP) 87±4.4 mmHg, heart rate (HR) 77±14 bpm). Clinic and ambulatory hypertension (systolic (S)BP ≥140 mmHg or diastolic (D)BP ≥90 mmHg) was present in 32% (SBP) and 40% (DBP) of subjects, respectively. Systolic hypertension differed from normotensives in terms of age (48.3±12.7 vs. 40.9±12.3 years, p<0.001), BMI (27.2±5.6 vs. 24.4±5.6 kg/m², p<0.001), smoking (30.0±4.3 vs. 19.7±4.2%, p=0.001), and IL1RL1 (rs1041973,CC/CA/AA) on IL1RL1 were genotyped by TaqMan probe method. HT was defined as SBP ≥140 and/or DBP ≥90 mmHg or current antihypertensive medications. We stratified all subjects into four groups according to gender and age (<49 or ≥50) and performed statistical analyses in each group. The effects of each SNP alone and combinations of two SNPs on HT risk were analyzed by using multivariate logistic regression models to estimate the strength of the associations by odds ratios (ORs) adjusted for age and body mass index (BMI). The OR of SNPs alone was calculated by using homozygous non-risk genotype as reference. To assess the joint ORs of the two genotypes combined for PON1 and IL1RL1 interaction, we subdivided the subjects into 9 strata according to cross-classified genotypes. We then obtained the ORs for each strata relative to the first stratum defined by non-risk genotype for both genes.

Results: Prevalence of HT showed that the risk genotypes for PON1 were minor homozygote (AA) in subjects aged <49 and major homozygote (GG) in subjects aged ≥50, while for IL1RL1 were minor homozygote (AA) in subjects aged <49 and ≥50. The ORs (95%CI) of homozygous risk genotypes were 2.39 (M 1.19-4.92) and 1.22 (F 0.65-2.25) and 1.66 (M 0.99-2.80) and 1.16 (F 0.72-1.92) and 1.39 (M 0.85-2.29) and 1.72 (F 1.16-2.54). In the 1.06 (F 0.50-2.18) and 1.97 (M 1.16-3.39) for IL1RL1 alone. The ORs (95%CI) of combined homozygous risk genotypes were 5.49 (M 4.97-6.01) and 1.06 (F 0.50-2.57) and 1.00 (M 0.52-2.57) and 1.00 (F 0.52-2.65).

Conclusions: SNP-SNP interactions between PON1 and IL1RL1 had significant effects as risk factors for HT development in men aged <49 and ≥50. However, the effect was prominent in men aged <49. SNP-SNP interactions between PON1 and IL1RL1 may contribute to young-onset hypertension in Japanese men.

P2097 | BEDSIDE
Synergistic effect of gestational hypertension and postpartum incident hypertension on cardiovascular health: a nationwide population study

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Aims: Gestational hypertension (GH) is a common complication of pregnancy and is associated with increased risk of incident hypertension in later life (IH) and cardiovascular events. However, the interactive effect of GH and IH on postpartum cardiovascular health remains unclear.

Methods and results: A nationwide population-based study was conducted using one million individuals from the Taiwan National Health Insurance database. Records from 1997 to 2009 were used to identify 1303 pregnant women with GH without previous cardiovascular disease. The control group comprised 5212 pregnant women without GH, matched for age and date of delivery. During the follow-up period (median duration, 5.8 years), 170 cardiovascular events developed. Women with GH had significantly higher risk of cardiovascular events (hazard ratio [95% confidence interval], 3.37 [2.84–4.58] and 3.40 [2.68–4.17]) than controls. Compared with women without GH or IH, there was a significantly higher risk of cardiovascular events for women without GH but with IH (relative risk [95% confidence interval], 2.24 [1.54–3.25]), women with GH but without IH (3.94 [1.87–8.32]), and women with GH and IH (14.75 [9.57–22.74]). The synergy index was 3.29 (95% confidence interval, 1.47–7.40), suggesting a positive interaction between GH and IH.

Conclusions: GH increased the risk of subsequent IH. Women with both GH and IH were more at risk of cardiovascular events than women with either GH or IH. The synergistic adverse effect of GH and IH on postpartum cardiovascular health indicates that more attention should be paid to this population.
**P2088 | BEDSIDE**

The “half marathon” of hypertension and diabetes: “the winner” of the 25 years’ long race in the Serbian cohorts of the seven countries study

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**Purpose:** In the presented analysis we focused on whether hypertension (HTA) arrives prior diabetes (DM) or vice versa, hoping to learn something new regarding cardiometabolic risk and its impact on specific vascular complications (cardio- and cerebro-v.).

**Methods:** The 3 Serbian cohorts were all men aged 40-59yrs at entry, subsequently followed every 5 years. Presence of DM and HTA and their progression over 25 year FU while studied aiming to assess their relationship and impact on cardiovascular and cerebrovascular mortality.

**Results:** 1552 men were divided in 4 groups based on HTA and DM presence (Table 1), while mortality data (Figure 1) showed the strongest positive correlation for HTA (irrelevant DM), in particular with cardiovascular mortality, while cerebrovascular mortality was steady over time. DM-influence was mild due to low percentage of DM.

<table>
<thead>
<tr>
<th>HTA total</th>
<th>Baseline</th>
<th>5y FU</th>
<th>10y FU</th>
<th>25y FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTA total</td>
<td>534</td>
<td>632</td>
<td>774</td>
<td>643</td>
</tr>
<tr>
<td>DM total</td>
<td>11</td>
<td>62</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>HTA+DM-</td>
<td>530</td>
<td>594</td>
<td>720</td>
<td>572</td>
</tr>
<tr>
<td>HTA-DM+</td>
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<td>9</td>
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<tr>
<td>HTA-DM-</td>
<td>4</td>
<td>38</td>
<td>54</td>
<td>71</td>
</tr>
<tr>
<td>HTA-DM+</td>
<td>25</td>
<td>43</td>
<td>194</td>
<td>39</td>
</tr>
</tbody>
</table>

**Conclusion:** In the Serbian cohorts of the SCS, as a result of the 25y FU, we have shown HTA appearing much earlier than DM and influencing cardiovascular mortality, in particular.

**P2089 | BEDSIDE**

The estimation of the vascular status parameters, depending on the gene polymorphism carrier of the angiotensin II receptor type 1 (AT2R1) and ethnicity of the patients with arterial hypertension (AH)

L. Goncharova1, A.Y. Postnov2, N.P. Sergutova1.

The estimation of the vascular status parameters, depending on the gene polymorphism carrier of the angiotensin II receptor type 1 (AT2R1) and ethnicity of the patients with arterial hypertension (AH) in the Serbian cohorts and its impact on specific vascular complications (cardio- and cerebro-v.).

**Methods:** Three groups: Moksha (n=50), Erzya (n=58) and Russian (n=48) patients with AH were formed. The results of two-factor analysis of variance allowed us to draw the conclusion about the certain influence of two factors on CAP (p=0.036) in female patients with AH – AT2R1 gene polymorphism and ethnicity.

**Conclusions:** Our data confirm a very high sodium consumption by Georgian hypertensive patients and their family members.

**Methods:** A total of 323 ethnically Georgians (127 males and 196 females, aged form 19 to 78 years) from 123 families were tested for salt-sensitivity using a high saline load in salt sensitivity in Georgian hypertensive patients. Moreover, among factors that determine salt-sensitivity endogenous cardiotonics (endothelin and marinobufagenin) have been considered. The second objective of our study was to determine the relationship between endogenous cardiotonic steroids and salt sensitivity in Georgian hypertensive patients and their family members.

**Conclusions:** Our data confirm a very high sodium consumption by Georgian hypertensive patients which is closely linked with a high incidence of salt-sensitive hypertension. Moreover, among factors that determine salt-sensitivity endogenous cardiotonic steroids (endothelin and marinobufagenin) have been considered. The second objective of our study was to determine the relationship between endogenous cardiotonic steroids and salt sensitivity in Georgian hypertensive patients and their family members.
LIPID LOWERING TREATMENT: NEW FINDINGS

P2102 | BEDSIDE
The effect of apolipoprotein E polymorphism on the response to lipid-lowering treatment with atorvastatin

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2 La Rabta University Hospital, Biochemistry, Tunis, Tunisia

Background: Statins are one of the most commonly prescribed classes of drug worldwide and therapy is highly effective in reducing low-density lipoprotein cholesterol (LDLc) levels and cardiovascular events. Despite these well recognized benefits, there is large variability in clinical response to statin treatment. These differences may be due to the interaction of environmental and genetic factors that affect drug bioavailability, receptor function or ligand structure.

Purpose: Our objective was to assess the effect of apolipoprotein E (ApoE) gene polymorphism on response to atorvastatin.

Methods: Our study included 60 consecutive patients, hospitalized for ACS (55.6±9.8 years, 86.2% men, 60.3% STEMl). DNA was extracted from leucocytes and analyzed by the PCR-RFLP protocol. Lipid profiles with a calculation of LDLc were performed before and 6 to 8 weeks after initiation of atorvastatin 40mg/day. We proposed a definition of resistance to atorvastatin (reduction in LDLc<20%) and then looked for correlations between clinical factors, the polymorphism of Apo E gene and the lipid response to atorvastatin 40mg/day.

Results: The average baseline LDLc was 1.13 g/l ± 0.4; baseline LDL cholesterol was lower in E4 carriers (-0.08). At the end of the follow up period the absolute reduction of LDLc was -0.35g/l ± 0.43 and the relative reduction of -23.90% ± 31.68. Resistance to atorvastatin was noted in 37.9% of patients. In univariate analysis, this resistance was inversely correlated with baseline LDLc (p<0.01). The E4 allele (ApoE) was associated with a higher risk of resistance (p<0.01). In multivariate analysis the studied polymorphism was not independently associated with response to atorvastatin and only the baseline LDLc was predictive of the response and of the resistance to atorvastatin.

Conclusion: This study objectified, in univariate analysis, a correlation between low baseline LDLc, poor response to atorvastatin, and ApoE allele. Multivariate analysis, however, calls into question the interest of genetic markers compared to the only baseline rate of LDLc to predict the resistance to atorvastatin.
as compared to higher values, significantly associated with a reduced risk of suf-
ferring a CVD event: HR 0.79 (95% CI 0.63-0.99) after full adjustment.

Conclusion: We demonstrate for the first time that serum PCSK9 concentrations are associated with future risk of CVD, independently from other cardiovascular risk factors.

P2105 | BEDSIDE

Effects of RG7652, a monoclonal antibody against proprotein convertase subtilisin/kexin type 5, on LDL cholesterol in patients with coronary heart disease or high risk: Results from the EQUATOR study

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Purpose: Proprotein convertase subtilisin/kexin type 9 (PCSK9) down-regulates high-density lipoprotein (LDL) receptors and plays a key role in cholesterol metabolism and coronary heart disease risk. RG7652 (MPSK3169A) is a fully human IgG1 monoclonal antibody (mAb) directed against PCSK9. This study evaluated the safety and LDL-cholesterol (LDL-c) lowering effects of RG7652 when added to standard of care therapy in patients with established coronary heart disease (CHD) or a high risk of CHD.

Methods: This international, double-blind Phase II study randomized patients to one of five dose regimens of RG7652, or placebo, given subcutaneously every 4, 8 or 12 weeks, for 24 weeks. The primary objectives were to evaluate the safety and efficacy of RG7652 for CHD or high risk of CHD in patients with baseline LDL-c between 90-250 mg/dL on standard of care therapy, including statin medications if tolerated. The modified intent-to-treat (mITT) population was used for efficacy analysis, and all patients who received at least one study treatment were included in safety analyses.

Results: 248 patients with median age 64 years (range 37-80), 43% women, were randomized in nine countries. At baseline, 52% of patients had established CHD, 46% were type-2 diabetic, 82% were on statins and the mean LDL-c was 126 mg/dL (3.3 mmol/L). On average, treatment with RG7652 reduced LDL-c by as much as 56-74 mg/dL (48-60%, p<0.001) from baseline to nadir for each of the dose regimens, as compared to placebo, with a dose-dependent magnitude and duration of effect. There were no unexpected safety findings, and the overall incidence of adverse events (86% and 88%) and serious adverse events (10% and 13%) were similar in the RG7652 arms (combined) and the placebo arm, respectively. The pharmacokinetics of RG7652 suggested target-mediated clearance.

Conclusions: RG7652 safely decreased LDL-c in patients with CHD or high CHD risk on standard of care therapy. The results of the EQUATOR study support further development of anti-PCSK9 monoclonal antibodies in Phase III lipid and cardiovascular outcomes studies.

P2106 | SPOTLIGHT

The ABCA1 agonist CS-6253 generates functional nascent HDL particles resulting in efficient cholesterol SR-BI delivery to hepatic cells and shows macrophage specific cholesterol mobilization and ather

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Background: CS-6253 is a selective 26 amino acid ABCA1 agonist peptide derived from the C-terminal of apoE with molar equi-potency to that of apoA-I, high stability and solubility. We investigated CS-6253’s ability to promote lipid transfer between nascent (n)HDL particles and plasma lipoproteins and examined cholesterol influx from remodelled HDL-like particles to hepatic cells through the SR-BI receptor. In addition CS-6253 properties were assessed in several animal models.

In vitro methods and results: nHDL-like lipoproteins from CS-6253 were generated by incubating CS-6253 in the presence of BHK cells expressing ABCA1 labelled with [3H]cholesterol and [3H] choline; native apoA-I was used as control. These nHDL particles were incubated with plasma at 37°C. CS-6253 increased LCAT activity significantly, although about 50% less efficiently than nHDL apoA-I (fractial esterification rate (FER) 11.40±0.045%/h vs. 22.32±0.86%/h, p<0.05). The majority of [3H] cholesterol from nHDL-CS-6253 was esterified by LCAT, resulting in an increase in ν1-migrating HDL-like particles in plasma. The phospholipid transfer protein (PLTP) promoted significant phosphatidylcholine transfer to apoB lipoproteins in vitro illustrating physiological remodeling in the presence of plasma lipoproteins. We then investigated cholesterol delivery from HDLs to hepatic tissue via SR-B1 using Fu5AH cells. The SR-BI-mediated cholesterol influx into Fu5AH cells was more efficient for HDL-CS-6253 (Km = 0.30±0.05 μM) than for HDL apoA-I (Km = 0.37±0.13 μM).

In vivo methods and results: In apoE KO mice significant increases in macrophage specific cholesterol mobilization to feces was found by a single 30mg/kg single free CS-6253 peptide ip injection compared to PBS control (+49%, p<0.01). In apoE KO mice made atherosclerotic by 14 week high-fat-diet CS-6253 ip treatment 25mg/kg/48h for 6 weeks reduced whole aorta atherosclerosis by (~34%, p<0.01). In rats CS-6253 showed an 8 hour half-life.

Conclusion: The ABCA1 agonist CS-6253 shows reverse cholesterol transport properties in vitro and potent anti-atherosclerosis actions in vivo. Given the high potency, high solubility and long half-life it is projected that CS-6253 can be ad-

P2107 | BEDSIDE

Effects of the CETP inhibitor evacarbazip administered as monotherapy or in combination with statins on mechanisms regulating LDL-c levels in patients with dyslipidemia

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Purpose: The CETP inhibitor evacarbazip (EVA) has been shown to significantly reduce LDL-c levels as monotherapy and in combination with statins. However, the mechanisms responsible for this reduction are not completely understood. We evaluated the mechanisms of EVA on mechanisms regulating LDL-c levels in patients with dyslipidemia.

Methods: Patients (n=398) with elevated LDL-c or low HDL-c in the multicen-
ter, randomized, double-blind, parallel, placebo-controlled trial were studied. Per-
cipications were from baseline in patients with anti-atherosclerosis actions in vivo.

Conclusions: For EVA monotherapy, statins alone, or EVA with statins (see Table). The effect of EVA on PCSK9 gene expression and secretion was also evaluated in vitro in a HepG2 cell model (+/−7652 expression).

Results: Statins alone increased PCSK9 (+29.4%, p<0.001), decreased lath-
osteral (-43.6%, p<0.001) and had no effect on camposterol levels. Results for EVA monotherapy and in combination with statins are shown in the Table. Lath-
osteral and camposterol levels were not affected by EVA monotherapy or in com-
bination with statins. Although EVA monotherapy increased PCSK9 levels, this increase was not dose-dependent and was partly due to a 6.8% decrease in the PBO group. Conversely, PCSK9 levels decreased when EVA was given alone. EVA monotherapy was associated with an increase in large LDL parti-
cles, whereas a decrease in small and very small LDL particles was observed with EVA in combination with statins. In vitro, EVA (at concentrations of ≥3.7 μM) dose-dependently decreased relative PCSK9 gene expression in HepG2 cells treated for 24hrs, and PCSK9 secretion from HepG2 cells at 24 and 48hrs in the presence or absence of mevastatin.

Conclusions: In patients with dyslipidemia, EVA monotherapy or in combina-
tion with statins did not significantly affect markers of cholesterol synthesis and synthesis. EVA monotherapy increased PCSK9 by 14.8% (6.3, 23.2, p=0.004), while EVA with statins reduced PCSK9 by 8.0% (14.0, -21; p=0.26).

P2108 | BENCH

High-density lipoprotein subfractions are associated with circulating monocyte subsets in patients with stable coronary artery disease

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Background: High-density lipoprotein (HDL) particles are highly heterogeneous in structure and the role of HDL subfractions in atherogenesis are not well un-
derstood. Recent studies, it has been suggested that small HDL (HDL-s) may be dys-
functional in patients with metabolic syndrome or coronary artery disease (CAD).

Monocytes and monocyte-derived macrophages are considered to play a key role in atherosclerotic diseases. Circulating monocytes can be divided into three sub-
types according to their surface expression of CD14 and CD16: pro- and anti-
flammatory subtypes. Our aim was to examine whether monocyte subsets are associated with HDL subfractions in patients with atherosclerosis.

Methods: We included 90 patients with angiographically stable CAD. Monocyte

Lipid lowering treatment: new findings 371

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subsets were defined as classical monocytes (CD14++CD16−; CM), intermediate monocytes (CD14+CD16+; IM) and non-classical monocytes (CD14+CD16++; NCM). HDL subfractions were measured by an electrophoresis method on poly-acrylamide gel.

Results: Patients with HDL-s levels in the highest tertile (HDL-s>1.3mg/dl; n=27; T3) showed the highest levels of pro-inflammatory NCM (14.7±7.7% vs. 10.7±5.5% and 10.8±5%; p<0.01) when compared with patients in the middle (HDL-s=0.9–12mg/dl; n=27; T2) and the lowest tertile (HDL-s<0.8mg/dl; n=26; T1). Additionally, patients in the highest HDL-s tertile showed lower CM levels than patients in the middle and lowest tertile (79.3±7% vs. 83.7±6% and 83.9±6%; p<0.01 for T3 vs. T2+T1). Levels of IM were not associated with HDL-s levels (5.9 ±3% vs. 5.6±3% vs. 5.3±3% for T3, T2 and T1, respectively). In contrast, intermediate and large HDL particles as well as total HDL were not associated with monocyte subset distribution.

Conclusion: High HDL-s levels are associated with an increase of pro-inflammatory NCM and a decrease of the more anti-inflammatory CM. This suggests that HDL-s could have dysfunctional anti-inflammatory properties in patients with established CAD.

IMAGING THE AORTIC VALVE AT THE TAVI ERA

P2109 | BEDSIDE
The progression of ascending aorta dilatation with both congenital bicuspid and non-bicuspid aortic stenosis
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Purpose: To describe the progression of ascending aortic (AscAo) dilatation in congenital bicuspid aortic valve (CBAV) and compare that with non-bicuspid aortic valve (NBAV).

Methods: There were 19,786 patients with at least one ECHO. Of these 234 had a CBAV (prevalence, 1.2%). Group 1 (n=258) comprised the CBAV. Group 2 was the NBAV (N=5,843). Patients in the NBAV with a mean aortic gradient (<5mmHg) were excluded. The Group 1, numbers are higher as a patient could progress from mild to moderate or severe to moderate severe AVS over the 14 years of data collection. The two groups were sub-divided into, mild, moderate or severe based on mean aortic valve area (AVG) according to the ASE guidelines. The AscAo maximal measurement was taken from the 3D images. ANOVA and Tukey-Kramer testing or a t-test was performed when appropriate.

Results: The CBAV show a statistically significant difference with ANOVA in the AscAo as the AVG Progressed. Tukey-Kramer testing indicated this was only significant between mild and moderate AVS. In the NBAV there was a progressive increase in the diameter of the ascending aorta which was also statistically significant. Similarly, Tukey-Kramer testing showed this was only significant between mild and moderate AVG. There were significant differences in the AscAo measurements between the CBAV and the NBAV for all severity grades. Those with NBAV are significantly older, see Table 1.

Table 1

<table>
<thead>
<tr>
<th>AS</th>
<th>Group 1. Bicuspid AS</th>
<th>Group 2. Non-bicuspid AS</th>
<th>N</th>
<th>Age</th>
<th>AVG</th>
<th>AscAo</th>
<th>N</th>
<th>Age</th>
<th>AVG</th>
<th>AscAo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (6–19mmHg)</td>
<td>196</td>
<td>47.0±15.1</td>
<td>8.6±4.3</td>
<td>35.6±6.3</td>
<td>5061</td>
<td>65.6±16.2</td>
<td>8.4±1.2</td>
<td>32.6±4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (20–40mmHg)</td>
<td>46</td>
<td>56.8±11.5</td>
<td>27±1.67</td>
<td>38±1.72</td>
<td>610</td>
<td>74.3±10.4</td>
<td>26.3±5.6</td>
<td>34±1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (&gt;40mmHg)</td>
<td>16</td>
<td>58.8±8.7</td>
<td>52.8±10.2</td>
<td>39±1.38</td>
<td>182</td>
<td>75.9±10.0</td>
<td>52.8±10.7</td>
<td>34.4±5.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANOVA</td>
<td>258</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.01</td>
<td>5843</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AVG, mean aortic valve gradient (mmHg); AscAo, ascending aorta (mm); AS = aortic stenosis.

Conclusions: For both CBAV and NBAV dilatation of the AscAo occurs when the AVG is mild to moderate, further increase in severity of AVG has no influence on the AscAo measurement. The pathology of the aortopathy is cystic medial necrosis in the younger CBAV and atherosclerosis in the older NBAV group. The rates of progression of AscAo dilatation are similar for both groups, however patients with CBAV start off with a significantly larger AscAo diameter.

P2110 | BEDSIDE
Aortic root geometry and its impact on measurements
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Background and aim: Aortic root (AoR) diameter measurements are usually performed in long-axis views by transthoracic echocardiography (TEE) and in coro- nal and sagittal slices by multidetector-gated computed tomography (MDCT). The usual TEE diameter obtained from one sinus of Valsalva (SV) to another yields slightly higher values than obtained from one SV to the opposite aortic commissure viewed by MDCT. We sought to assess the accuracy of TEE in the evaluation of AoR dimensions compared with MDCT, and the potential influence of AoR geometry on these measurements.

Methods: Sixty patients (mean age: 65±11; 54% men) with a severe aortic valve disease (stenosis or regurgitation) were evaluated with TTE and MDCT for AoR measurement. Three different echocardiographic methods were used: leading-edge-to-leading edge, inner-to-inner and outer-to-out and results were compared with those obtained by MDCT. MDCT measurements from one SV to another were also compared with measurements from each SV to the opposite commissure. Asymmetry was considered if one diameter was ≥10% larger than the subjacent measurement.

Results: The three methods showed excellent interobserver and intraobserver variability and reproducibility. The leading-edge-to-leading edge method showed the best agreement with MDCT (Table 1). AoR was asymmetric in 5 patients (8.3%), 4 of whom had bicuspid aortic valve. No relationship was found between mean diameters (40mm) and asymmetry.

Conclusions: TTE is an accurate technique for the assessment and follow-up of AoR diameters in valve patients. The leading-to-leading approach is that which shows the best agreement with MDCT measurements of AoR dimensions. Asymmetry of the AoR may lead to the largest AoR diameters. The presence of asymmetry is independent of aortic diameters, but closely related to valve morphology.

P2111 | BEDSIDE
Prognostic value of projected aortic valve area in patients with paradoxical low-flow low-gradient severe aortic stenosis: Japanese Multicenter Aortic Stenosis (JUST) Study
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Purpose: We hypothesized a subset of patients with paradoxical low-flow, low-gradient severe aortic stenosis (PLFLG-SAS) despite preserved ejection fraction might be pseudo-severe AS due to low-flow status, and the measurement of projected aortic valve area (AVAproj) could discriminate from true-severe to pseudo-severe AS.

Methods: 3D stress echocardiography was performed in 61 patients with PLFLG-SAS (AVA ≤1.0cm²; stroke volume index <35ml/m²; mean pressure gradient (PG) <40mmHg). Stroke volume was determined by 3D volumetric method. AVA was plotted against transvalvular flow (Q) at each stage; valve compliance (VC) was derived as a slope of the regression line fitted to AVA versus Q plot. AVApro was calculated as AVArest×VC×250 (Crest). The primary endpoints were cardiac death (CD) and major adverse cardio-cerebrovascular events (MACE).

Results: Of these, 27 (44%) patients had AVAproj <1.0cm² (true-severe AS) and 34 (56%) had AVAproj ≥1.0cm² (pseudo-severe AS). During a mean of 420-days follow up, MACE developed 23 patients (37.7%) including 6 CD (9.8%). Kaplan-Meier analysis showed that the pseudo-severe AS had a significantly higher survival rate than the true-severe AS (p=0.045, Figure). Cox proportional-hazard analysis revealed that AVAproj was an independent predictor for MACE (hazard ratio: 0.27, p=0.013).

Conclusions: More than half of Japanese PLFLG-SAS patients revealed pseudo-severe AS using AVAproj. This is one possible reason why Japanese PLFLG-SAS has a better prognosis compared to Western countries.

P2112 | BEDSIDE
Echocardiographic predictors of pulmonary hypertension in patients with severe aortic stenosis

Purpose: Pulmonary hypertension (PH) is associated with adverse outcomes in
different cardiac diseases. Thus, in severe aortic stenosis (SAS), the development of PH may have impact in prognosis, but its prevalence is largely unknown as well as the underlying mechanisms. The aim of this study is to determine the prevalence of PH in patients with SAS and to find echocardiographic predictors of pulmonary artery systolic pressure (PASP).

Methods: We retrospectively studied consecutive patients, included between February 2008 and December 2012, with isolated SAS diagnosed by conventional echocardiography-Doppler, using the EAE criteria for severity. Patients with non-sinus rhythm, ejection fraction <50% and inconclusive assessment of PASP were excluded. In all patients we assessed: left ventricle (LV) end-diastolic and end-systolic dimensions and wall thickness, fractional shortening, left and right atrium diameters, biventricular ejection fraction and PASP. LV diastolic function was classified in normal pattern, impaired relaxation, pseudonormal and restrictive, according to the EAE guidelines and the transmitral flow (E and A velocities and E deceleration time), pulmonary venous flow (S/D) and mitral annulus velocities (E’, A’). E/E’ was determined in a subgroup of patients.

Results: We included 243 patients (110 male, 73±12 year-old). Moderate to severe PH (PASP ≥45 mmHg) was found in 29% of the population. In 74% of patients, diastolic dysfunction patterns were found. PASP was correlated with left atrial dimension (R=0.29, P<0.04), mitral inflow velocities E (R=0.41, P<0.001), A (R=0.33, P=0.02), E/A ratio (R=0.44, P<0.001) and E deceleration time (R=0.29, P<0.037). Moreover, more severe degrees of diastolic dysfunction had higher values of PASP. In a subgroup of 92 patients, we found a significant correlation between PASP and E/E’ ratio (R=0.67, P<0.001).

Conclusions: Our findings suggest that echocardiographic markers of diastolic dysfunction are predictors of PH, thus emphasizing its role in the genesis of PH in SAS. Its prognostic value will be evaluated in a future prospective trial.

P2113 | BEDSIDE
Impact of energy loss index on left ventricular mass regression after successful transcatheter aortic valve implantation

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Background: The energy loss index (ELI) currently has been utilized as new functional index to assess the severity of aortic stenosis (AS). The aim of this study was to investigate the effect of the ELI on left ventricular mass indexed (LVMI) regression in patients after successful transcatheter aortic valve implantation (TAVI).

Methods: A total of 33 patients with severe AS who successfully underwent TAVI with Edwards Sapien XT bioprosthesis was studied. Transthoracic echocardiography (TTE) was performed before TAVI and 6 months later (post-LVM) (n=33). The ELI was calculated as [(effective orifice area (EOA) x aortic cross sectional area)/ (aortic cross sectional area- Pressure recovery)] divided by the body surface area (BSA). The LVMI regression rate (%) was calculated as 100 x (post-LVM minus pre-LVM)/ (pre-LVM). A cardiac event was defined as composite of death requiring hospitalization or cardiac death.

Results: LVMI indexed regressed significantly (146.7±43.8g/m² to 131.2±36.8g/m², P<0.008) at 6 months after TAVI. The ELI increased from 0.46±0.10 to 0.96±1.14 cm²/m², P<0.005. The dimensionless index (DI) also increased significantly (0.09±0.04 to 0.49±0.1, P<0.005). The LVMI regression rate negatively correlated with the ELI (R=-0.7, P<0.001). By receiver operating characteristic (ROC) curve analysis, ELI ≤1.14cm²/m² predicted smaller (≤55%) LVMI regression rates. Patients with ELI ≤1.14cm²/m² had significantly lower cardiac event-free survival.

Conclusions: The ELI could predict LVMI regression after successful TAVI with Edwards Sapien XT bioprosthesis. It is still uncertain whether the ELI is a stronger predictor of clinical events than other indices, and further larger scale study is needed to elucidate the clinical impact of ELI in patients with TAVI.

P2114 | BEDSIDE
Transcatheter aortic valve implantation in patients with left ventricular dysfunction: does basal two-dimensional strain have predictive value?


Introduction: Severe aortic stenosis associated with left ventricular systolic dysfunction (LVSD) poses a risk for conventional aortic valve replacement. Transcatheter aortic valve implantation (TAVI) is an alternative treatment for these patients. The aim of the study was to analyse changes in left ventricular ejection fraction (L VEF) and LVSD after TAVI (AVAI) to evaluate the impact of LVSD on global left ventricular longitudinal systolic strain (GLS) and ascertain which parameters predict L VEF improvement after TAVI.

Methods and results: 130 patients were selected for TAVI because of inoperable severe aortic stenosis. LVSD was present in 33 (25.4%). Mean age was 77.7±10.5 years. Technical approach was transapical, transapical and transaortic in 51.5%, 36.4% and 12.1% of cases respectively. L VEF was measured using the biplane Simpson’s method and GLS was obtained by speckle-tracking analysis. Before implantation, L VEF was 39.1±9.2% and GLS -9.9±2.8%. Immediately after the TAVI procedure, L VEF improved significantly (43.9±9.7%, p=0.001) but GLS did not (10.3±12.9%, p=0.538). After a mean follow-up period of 1.8±1.4 years, L VEF also showed a significant improvement compared to the basal situation (46.7±11%: p=0.008), but was not significant compared to the immediate post-implantation (-10.3±2.9%; p=0.538). GLS improved significantly compared to basal situation (-13.5±4.5%: p=0.044). Comparison of basal GLS <9% (N=19) versus GLS ≥9% (N=14) is shown in the attached table.

Comparison of basal GLS (<9% vs ≥9%)

<table>
<thead>
<tr>
<th>GLS ≤9% (n: 14)</th>
<th>GLS ≥9% (n: 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L VEF (% pre-TAVI)</td>
<td>33.8±8.3</td>
</tr>
<tr>
<td>L VEF (% post-TAVI)</td>
<td>37.0±9.1</td>
</tr>
<tr>
<td>GLS (%) immediate post-TAVI</td>
<td>-8.8±1.7</td>
</tr>
<tr>
<td>GLS (%) immediate post-TAVI</td>
<td>-16.8±5.2</td>
</tr>
<tr>
<td>GLS (%) long-term follow-up</td>
<td>-11.0±5.2</td>
</tr>
</tbody>
</table>

Conclusions: Patients with aortic stenosis with LVSD presented a significant improvement in GLS one year after TAVI. Pre-TAVI GLS <9% was associated with a greater increase in left ventricular ejection fraction after the procedure. Thus, GLS may provide additional information for TAVI candidate selection.

P2115 | BEDSIDE
Measurement of energy loss index in recommendation of tricuspid aortic stenosis without significant left ventricular hypertrophy

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Background: Continuous wave Doppler echocardiographic transaortic pressure gradient may be sometimes overestimated in patients with aortic stenosis (AS). Pressure recovery phenomenon is caused if kinetic energy is converted to potential energy at the downstream of the stenotic aortic valve, and this phenomenon occurs in some patients with AS, causing the overestimation. Thus, it is recommended to use the energy loss index (ELI) for the assessment of AS in such a circumstance. AS is frequently associated with left ventricular hypertrophy (LVH) which is a major compensatory mechanism in response to pressure overload. However, it is unclear whether there is a relation between pressure recovery and LV hypertrophy (LVH) in patients with AS.

Purpose: We aimed to compare the differences in Doppler measurement of pressure recovery between patients with tricuspid and bicuspid AS, and to explore the relationship between pressure recovery phenomenon and the presence of LV hypertrophy (LVH).

Methods: We retrospectively studied 105 patients with ages of 60 years or older who underwent aortic valve replacement for AS. Aortic valve was tricuspid in 86 patients and bicuspid in 19 patients. Echo measurements were conducted before surgery. We used the continuity equation to measure the aortic valve area index (AVAI) and calculated the pressure recovery between patients with LVH and without LVH.

Results: An index of relative discrepancy between ELI and AVAI, (ELI−AVAI)/AVAI was significantly greater in patients with tricuspid aortic valve (0.18±0.10 vs 0.13±0.04, p<0.05). (ELI−AVAI)/AVAI was greater in patients without significant LVH than in those with LVH among those with tricuspid severe AS (0.18±0.11 vs 0.14±0.05, p<0.05). (ELI−AVAI)/AVAI was greater in patients without significant LVH than in those with LVH among those with bicuspid severe AS (0.15±0.04 vs 0.11±0.03, p<0.05).

Conclusions: Pressure recovery was greater in patients with tricuspid aortic valve than in those with bicuspid aortic valve and was greater in tricuspid aortic valve patients without LVH than in those in significant LVH. Thus, it is recommended to measure both AVAI and ELI if the patients have tricuspid aortic stenosis without significant LVH.
2132 | BEDSIDE
Predictors of effectiveness and complications of cardiac implantable electronic devices lead extraction in patients with systems older than 10 years
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Background: Many studies have clearly identified the risk factors of CIED leads extraction (LE). The outcome of patients with multiple old leads is not yet clearly known.

Methods: Patients with IA or B indication for LE of PM or ICD leads more than 10 years after first implant, were randomized to use either mechanical extraction only or a combination of mechanical extraction and excimer laser technique. The primary endpoint was the efficiency and safety of the extraction procedure.

Results: 227 pts (141 M, 86 W, mean age 64±21 years) with sepsis and evidence of bacterial endocarditis (139) or defect in the PM/ICD pocket (88). The average time from the first implant of the electrodes (EL) was 147±29 months. The group included 121 ICD EL (97 dual coil), 89 atrial and 181 ventricular pacemaker leads. The mean dwell time was 28.2 (ranged 3-58) months. 6 leads with time less than 24 months since implantation presented outer insulation damage-BAP (22,5±3 months). The mean number of implanted leads was 1.6 (ranged 1-2), the mean dwell time was 28.2 (ranged 3-58) months. 6 leads with time less than 24 months since implantation presented outer insulation damage-BAP (22,5±3 months). The mean dwell time was 28.2 (ranged 3-58) months. 6 leads with time less than 24 months since implantation presented outer insulation damage-BAP (22,5±3 months). The mean dwell time was 28.2 (ranged 3-58) months. 6 leads with time less than 24 months since implantation presented outer insulation damage-BAP (22,5±3 months).

The results of the extraction procedure were as follows: Complete extraction was achieved in 212 patients (93%), no patient died immediately, 30-days mortality rate was 4.85%. Complications occurred in 7.48% of patients. Predictors of complications are summarized in Table 1.

Conclusions: The presence of multiple electrodes, use of mechanical LE only, dual coil ICD leads, sepsis, renal failure and short-term operator experience were strongly associated with procedure complications.

2133 | BENCH
Optim insulation failure in transvenously extracted implantable cardioverter-defibrillator leads
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Purpose: Optim insulation is believed to present increased durability, improved lubricity and flexibility comparing to both silicone and polyurethane insulations. The aim of the study was to analyze the outer Optim insulination morphology.

Methods: 11 consecutive patients (pts.) (9 male) underwent transvenous lead extraction because of chronic pocket infection (CPI) (2/11), infective endocarditis (IE) (1/11), both CPI and IE (3/11) and non-infective indications (5/11 pts.). The mean patients age was 62.6 years (ranged 46-73). 11 Optim leads were analysed with optical microscope and scanning electron microscope.

Results: The mean number of implanted leads was 1.6 (ranged 1-2), the mean number of procedures until removal was 1.2, the mean time from the last procedure was 22.5 (ranged 3-46 months), the mean dwell time was 28.2 (ranged 3-58) months. 6 leads with time less than 24 months since implantation presented outer insulation failure: the youngest 3 months old. The type insulation failure was similar to the silicone insulation (0), biofilm formation (1), stress cracking of polyurethane (P) and abrasion (A). 9/11 presented BPA in the intracardiac part, 9/11 BPA intravenously, 2/11 BPA, 2/11 A, 2/11 B were noticed in the pocket.

Conclusions: The outer Optim insulation may undergo biodegradation aggra-vated by wear leading to abrasions. Lead insulation failure was observed in infective and non-infective complications, and may appear even 3 months since implantation.

2134 | BEDSIDE
Dry late heart wall perforation with icd lead - in most of patients the cardiac surgery can be avoided
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The goal: Analysis of perforating ICD leads extraction safety.

Methods: TEE & TTE and other preoperative findings were analyzed.

Results: We have extracted 2574 ingrown leads from 1536 patients; in 390 due to infection (39,4%) or different form of lead dysfunction (63,6%). In 86 pts (22%) different forms of perforation of RVA with ICD lead. ECHO: dry perforation (tip in epicardial space, no fluid) 64 (74%), small “flea” of dense fluid round the lead tip 6 (7%), wet perforation (thin layer of fluid 5 (6%), deep subepicardial tip pene-tration 4 (5%) but in 3 (%) of pts diagnosis was based on other symptoms (P/I/abnormalities). Indications for TEE: “lead dysfunction” (P/I/abnormalities) 54 (62%), diagnosed perforation 13 (15%) and infection 13 (15%). In most pts has late perforation or late diagnosed asymptomatic perforation; Time implantation – diagnosis: aver51,0 (1-146) mth; < 3 mth; 4; 3, my2year: 17; 2-5y; 35, > 5y; 35, in 59/86 (69%) over 3 y. All perforating leads were extracted and it made possible to open of open-chest surgery in all pts of all pts. But surgery was necessary in 72 cases between two pts, with complications, perforation caused by RVA was not successful. Impres-sion: during repetitive ICD lead implantation we have to avoid of previous tip location region because renewed perforation is possible (lead may to wander into old channel).

2135 | BEDSIDE
Transvenous removing of pacing and ICD leads: single italian referral center experience
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Introduction: Device related complications are rising the need of Transvenous Lead Removal (TLR), Transvenous extraction of Pacing (PL) and Defibrillating Leads (DL) is a highly effective technique. Aim of this report is to analyse the longstanding experience performed in a single Italian Referral Center.

Methods: Since January 1997 to December 2013, we managed 2113 consecu-tive patients (1611 men, mean age 65.4 years) with 3843 leads (mean pacing period 71.1 months, range 1-420). PL were 3144 (1522 ventricular, 1303 atrial, 319 coronary sinus leads), DL were 699 (678 ventricular, 6 atrial, 15 superior vena cava leads). Indications to TLR were infection in 83% (systemic 28%, loco-ral 55%) of leads. We performed mechanical dilation using a single polypropylene sheath technique (Cook Vascular – Leechburg PA, USA) and if necessary, other intravascular tools (Catchers and Lassos, Osypka, Grentzig-Whylen, G); an attempt to remove all the free-floating leads or failure of the standard approach.

Results: Removal was attempted in 3634 leads because the technique was not applicable in 9 PL. Among these, 3572 leads were completely removed (98.0%), 38 (1.0%) partially removed, 39 (1.0%) not removed. Among 3748 exposed leads, 587 were removed by manual traction (15.6%), 2799 by mechanical dilation using the venous entry site (74.7%), 25 by femoral approach (FA) (0.7%) and 252 by VA (7.0%). All the free-floating leads were completely removed, 26.5% by FA and 72.5% by VA. Major complications occurred in 12 cases (0.56%): cardiac tamponade (11 cases, 2 deaths), hemotorax (1 death).

Conclusions: Our experience shows that in centers with wide experience, TLR using a single sheath mechanical dilation has a high success rate and a very low incidence of serious complications. TLR through the Internal Jugular Vein increases the effectiveness and safety of the procedure also in case of free-floating or challenging leads.
2136 | BEDSIDE
Dry heart wall perforation - the new epimy of better diagnosed old phenomenon ?
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1Medical University of Lublin, Department of Cardiology, Lublin, Poland; 2Medical University of Lublin, Department of Cardiac Surgery, Lublin, Poland

Theoretically increased risk of dysfunctional perforating lead extraction inclined us for attempt to localise tip of lead in relation to epicardium and the commonness of complications (postoperational to perforation was surprising).

Goal: Retrospective analysis computer data-base referential centre of transvenous lead extraction (TLE) in our country. TEE & TTE and other preoperative findings were analyzed. We have extracted 2574 ingrown leads from 1536 patients; 216 leads presented signs of perforation (8% of leads & 14% of PM leads).

Results: ECHO: dry perforation (tip in epicardial space, no fluid) – 168 (79.6%), small lens of dense fluid round the lead tip – 17 (8%), wet perforation (thin layer of fluid – 26 (12.3%), deep subepicardial tip penetration – 15 (7%) but in 23 (11%) of pts diagnosis was based on other symptoms. Indications for TLE: “lead dysfunc- tion” (pacing/sensing impedance abnormalities) – 108 (51.2%), diagnosed perforation 47 (22%), infection – 28 (13%), other – 26 (12%). In 11 pts all parameters of pacing/sensing/impedance were normal (5%) but in other drop of sensing (7%) or sizzles (13) were noted (40%) rise of Pih in 107 or loss of pacing (23) were observed (82%) and rise in 77 or drop in 15 of impedance (44%) were noted in different combinations. In 24 of PM pts Pih was lower in BP than UP configuration. Subjective symptoms (in 41/21121% only): 28 atypical chest pain, “pacing intolerance” 6, extracardiac pacing 5. Perforating lead tip localization: RVA 166, ICD 331. Lead perforating lead model: PM BP-172, ICD HR-585, PM UP-13. Active fixation 98, passive –113. Time implantation – diagnosis: aver.66.5-(1.316)

Conclusions: The presence of fibrotic adhesions was frequently associated with the tip of lead must to be search using additional projections. Pacing / sensing / impedance parameters abnormalities may to guide for proper diagnosis. It gradual deterioration seems to be most frequent but non-specific symptoms.

2137 | BEDSIDE
Utility of the mechanical systems for transvenous lead extraction. The analysis of experience with extraction of 2574 permanently implanted leads in 1536 pts
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Necissity for transvenous lead extraction (TLE) rises using two basal techniques: mechanical and energy delivering systems. The first, is counted as safer but less effective. The aim: analysis of the effectiveness & safety of mechanical systems for TLE.

Methods: We have extracted 2574 ingrown (PM >12, ICD >6 mths) leads in 1536 pts. (61.1% M) mean age 64.6y, with PM and ICD systems. 72.7% leads were in PM, 27.3% in ICD. ARA perforating lead model, PM BP-172, ICD HR-585, PM UP-13. Active fixation 98, passive – 113. Time implantation – diagnosis: aver.66.5-(1.316)

Conclusions: The presence of fibrotic adhesions was frequently associated with the tip of lead must to be search using additional projections. Pacing / sensing / impedance parameters abnormalities may to guide for proper diagnosis. It gradual deterioration seems to be most frequent but non-specific symptoms.

2140 | BEDSIDE
Riata lead extraction: technical approach and procedural implications of transvenous removal

Background: Percutaneous removal of implantable defibrillator (ICD) leads re-
mains a difficult procedure, despite the fact that extraction techniques have been improved and advances in lead technology have been made in order to reduce fibrous tissue growth along the lead, thereby easing extraction. We evaluated the effectiveness and safety of a mechanical single-sheath extraction technique, described the occurrence and location of fibrous adhesions detected during the procedure, and investigated the relationship between the presence of adhe-
sions and patient and lead characteristics.

Methods and results: We studied 545 consecutive patients who underwent transvenous extraction of 582 ICD leads from 1997 to 2012. Our technique achieved a success rate of 99%, causing no major complications. Fibrotic ad-
hesions were found during removal of 547 leads requiring mechanical dilatation. Areas of adherence were in the subclavian vein (78%), the innominate vein (64%), the superior vena cava (65%) and the heart (73%). Dwelt-time, passive fixation and dual-coil lead design were independently associated with adherences. Dual-coil lead design was associated with adherence in the innominate vein and in the superior vena cava, coil treatment (expandable polytetrafluoroethylene-coated or medical adhesive back-filled coils) prevented adherences in the superior vena cava, and the passive fixation mechanism was associated with adherences in the heart.

Conclusions: Mechanical single-sheath extraction of ICD leads proved safe and effective. The presence of fibrotic adhesions was frequently associated with longer lead dwell-time, passive fixation and dual-coil lead design. By contrast, the use of treated coils prevented intravenous adherences.

2139 | BEDSIDE
Efficacy and feasibility of cardiovascular implantable electronic devices lead extraction in elderly patients
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Background: In contemporary practice, the proportion of elderly individuals in the population is growing and the need for percutaneous transvenous lead extraction in elderly patients has been increasingly required. The elderly have more risk factors than younger patients needing lead extraction. However, the safety of lead extraction for elderly patients remains unclear.

Methods: Between 2005 and 2013, we collected data of 250 consecutive pa-
tients who underwent percutaneous transvenous lead extraction and compared incidence of major adverse events (MAE: death, myocardial infarction, stroke, dual-coil lead removal, pulmonary embolism, blood transfusion or pneumomediastinum) between patients <80 years and patients ≥80 years old. The primary endpoint of this study was incidence of MAEs after procedure. The secondary endpoint was hospitalization period.

Results: There were 68 patients (27.2%) with age ≥80 years and 182 patients (72.8%) with age <80 years. The most common indication for lead extraction in elderly patients was infection (97.1%). All patients underwent successful transvenous removal of endocardial leads. Two of 68 patients (2.9%) had evidence of MAE in elderly patients. No significant difference of MAE was found in the elderly group (2.9 vs. 2.2%; P=0.921). There was no difference in hospitalization period between those age ≥80 years and age <80 years (37.9±31.3 days vs 31.4±27.4 days, P=0.105).

Conclusions: In elderly patients, percutaneous transvenous lead extraction could be performed safely without prolonged hospital stay.
and Drug Administration because of an increased rate of failure due to conductor fracture or insulation abrasion. Treatment options include intensifying monitoring and possible recalled lead replacement, with or without extraction. According to lead design and type of failure, procedural extraction complexity may be different.

Aim of this study was to assess the extraction profile of R leads with and without cable externalization in comparison to S leads.

Methods: From January 1997 to December 2012, we included in the analysis all the consecutive R and S leads extracted transvenously.

Results: Among 545 consecutive patients with 582 transvenous ICD leads extracted, we identified 51 S (S Group) and 102 R (R Group). Indications to remove were infective in the majority of cases (70%) and with a prevalence of dual coil leads (90%). Baseline patients and lead characteristics resulted comparable between both groups.

Success rate was very high in both groups (100% S leads vs 99% R leads, p<0.05) without major complications. R leads required more often MD (98% vs 92%, p=0.05) and larger sheaths, a more frequent crossover to the transjugular approach (ITA) (8% vs 2%, p=0.10), and a final longer extraction time (11 ± 13 vs 18 ± 23 min): Overall, the rate of complex extraction procedures (CEP) resulted higher in the R Group (32% vs 14%, p=0.02). Presence of cable externalization was a major independent predictor of difficult extraction and necessity of ITA.

Conclusions: Extraction of R leads is feasible and effective. However, extraction of R leads is more complex than S leads. Lack of coil backfilling and cable externalization in R group may account for these differences. The decision to extract or not to extract R leads should be carefully individualized.

2141 | BEDSIDE

Transvenous lead extraction - more risky in cases with non-infective indications?

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There is considerable controversy regarding different safety of transvenous lead extraction (TLE) in relation to procedure indications and non-infective are some time recognized as more risky. Objective: Analysis of safety and feasibility of TLE in our material.

Methods: We have extracted 2167 ingrown endocardial leads from 1283 patients within the last 7 years. We analyzed complications and technical problems related to percutaneous lead removal procedures referring these problems to three (different indications) groups.

Results:

- **Number of patients/procedures**
  - Local pocket infection: 330
  - Lead-dependent endocarditis: 224
  - Non-infective indications: 79
  - Total: 633

- **Age of pts**
  - 68.7 (13.7) years
  - 65.3 (14.8) years
  - 62.2 (17.8) years
  - **p<0.001**

- **Sex-females %**
  - 89 (27.0%)
  - 73 (32.6%) 1327 (44.9%)

- **Number of leads extracted (mean) (SD)**
  - 1,95 (0.76)
  - 2,21 (0.85)
  - 1,46 (0.74)
  - **p=0.032**

- **Average implant duration - in months**
  - 72.3 (54.5)
  - 65.4 (62.8)
  - 87.3 (64.7)
  - **p=0.002**

- **Number of procedures before extraction**
  - (mean) (SD)
  - 2,19 (1,18)
  - 2,28 (1,46)
  - 1,74 (1,09)
  - **p<0.001**

- **Full radiological success (%)**
  - 317 (96.3%)
  - 206 (92.0%)
  - 687 (94.2%)

- **Technical problems during TLE (%)**
  - 46 (13.9%)
  - 40 (17.8%)
  - 123 (16.9%)

- **Major complications (%)**
  - 1 (0.3%)
  - 5 (2.2%)
  - 13 (1.8%)

- **Minor complications (%)**
  - 3 (0.7%)
  - 73 (32.6%)
  - 16 (2.2%)

- **Procedure related death**
  - 0 (0.0%) 0 (0.4%)

Impression: TLE in pts with local pocket infection seems to be very slightly more effective and safe. It may be explained by lower percentage of female pts. Higher percentage of complications in both another groups can be explained with longer implant duration, higher percentage of female pts. and toxemia.

Conclusions: There is no simple relation between TLE effectiveness/safety and main indication to the procedure.

VASCULAR CELLS AND NEW VESSELS

2140 | BENCH

Acetyltransferase Gcn5 triggers Nox2 upregulation and oxidative stress in diabetes


The main indication to the procedure.

Shh signaling is critically involved in neointimal lesion formation by differentiation of vascular progenitors in the adult. Aim of the study was to determine the role of Shh in orchestrating the response of the adventitia to vascular injury. Methods and results: Wire-mediated endovascular injury of the femoral artery was performed in C57BL/6 mice to induce neointimal lesion formation. Staining for K-ED showed that the majority of proliferating cells were located in the adventitial layer. Shh was significantly up-regulated in proliferating cells as well as in the intimal lesion at 4 and 7 days after injury compared to sham-operated arteries, as determined by qPCR and immunohistochemistry (IHC). Moreover, we determined a strong correlation in the expression of Shh and its receptor Ptc1 fibroblasts in the adventitial regions of injured aortas. Expression of Shh and its receptor were increased in diabetic fibroblasts compared as plaques to healthy mammalian arteries using IHC. In vitro, stimulation of human adventitial fibroblasts (AAoF) with Platelet-derived growth factor-BB resulted in a significantly increased expression of Shh and its receptor Ptc1. Incubation of AAoF and human coronary artery smooth muscle cells (HCAVMSC) with recombinant Shh dose-dependently induced cell proliferation and migration. The specific Shh inhibitor DCC-0449 (Vismodegib) was not only effective in attenuating Shh signaling but also prevented the Shh induced functional effects in AAoF in a dose-dependent manner. Following wire-induced injury, local application of DCC-0449 via a self-degrading Pluronic® F-127 Gel significantly reduced neointimal lesion formation (neointima/media ratio: 2.19 ± 0.29 vs. 1.87 ± 0.24, p<0.05). This was associated with a reduced proliferation of total cells and in particular adventitial cells. Interestingly, Shh-expressing and proliferating cells in the adventitia were identified as Sca-1+ cells suggesting Shh as a critical regulator of perivascular stem cell function during neointimal lesion formation. The effects of Shh inhibition on the downstream signaling pathways are currently investigated.

Conclusions: Shh signaling is critically involved in neointimal lesion formation by augmenting vascular cell proliferation and as a potential regulator of perivascular stem cell function. Therefore, these data add significantly to our understanding of vascular proliferative diseases.

2150 | BENCH

Effect of autophagy deficiency in smooth muscle cells on vascular function


Autophagy is a subcellular housekeeping mechanism which is essential for optimal cellular function by ridding the cell of damaged proteins and organelles. Although autophagy deficiency in cardiomyocytes leads to heart failure, very little is known about the importance of this process in smooth muscle
Vascular cells and new vessels

2151 | BENCH
Sphingosine-1-phosphate receptor 1 (S1P1) promotes vascular remodeling via interleukin-6 (IL-6) after vascular injury in mice
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Purpose: Sphingosine-1-phosphate (S1P) is a bioactive sphingolipid mediator that mediates diverse cellular responses including cell proliferation, survival, and migration. In clinical setting, serum S1P concentration was known to a predictive marker for the presence and severity of obstructive coronary artery disease in human. However, due to the large number of S1P receptor (S1PR) family members, S1P-specific G-protein coupled receptors (S1PR1-S1PR5). According to recent study, expression of S1PR1 is elevated in tumor cells and this elevation contributes to interleukin-6 (IL-6) gene upregulation, thereby accelerating tumor growth and metastasis. Vascular inflammation and smooth muscle cell proliferation contribute to vascular remodeling and obstructive vasculopathies such as atherosclerosis and restenosis following angioplasty. However, pathophysiological roles of S1P and S1PR1 in atherosclerosis are not known. Here we examined whether S1P could be involved in the development of neointima formation.

Methods and results: We performed unilateral carotid artery ligation in male C57BL/6 mice. 4 weeks after carotid artery ligation, neointima formation was confirmed. S1PR1 mRNA expression was 1.4 folds higher in injured arteries than in control. Next, we generated mice that overexpressed S1PR1 (Tg-S1PR1) under the control of a smooth muscle actin promoter. Tg-S1PR1 and nTg mice were subjected to carotid artery ligation. After 4 weeks following this intervention, In/Control/Media ratio was significantly increased in Tg-S1PR1 mice compared with nTg mice (0.76±0.16 vs. 2.05±0.05, P<0.001). These results indicate that TF is chaperoned by PDIA2 to the cell migratory front when migration is initiated. Absence of PDIA2 silenced cells show cell-surface expression is significantly reduced in PDIA2-silenced-HVSMC and precipitation of TF shows a direct interaction TF-PDIA2 in the cell surface. Further, we determined the expression level of TF in PDIA2 silenced-HVSMC and PDIA2 silencing in vivo implants of PDIA2 silenced-HVSMC to the neointima formation via IL-6 after vascular injury.

2152 | BENCH
Exercise promotes post-ischemic collateral artery growth mediated by inducible nitric oxide expression of monocytes
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Background: Collateral artery growth (arteriogenesis), an important adaptive response to hampered arterial perfusion, reduces cardiovascular mortality. The effects of physical exercise on arteriogenesis, particularly the role of nitric oxide derived from spleen and bone-marrow-derived mononuclear cells, are hitherto unknown.

Methods and results: After three weeks of voluntary treadmill exercise (daily running distance 5.5±1.0km), ligation of the left femoral artery was performed in C57BL/6 mice. Hindlimb perfusion as assessed by Laser Doppler Imaging (LDI) immediately after surgery did not differ from sedentary mice. However, prior exercise improved hindlimb perfusion restoration up to seven days after femoral artery ligation, also when exercise was stopped at the time of ligation (perfusion restoration to 52.6±4.1% of non-ligated control versus 34.8±2.0% in sedentary animals, p<0.001). This was accompanied by an accumulation of angiogetic macrophages and increased expression of endothelial (eNOS) and inducible nitric oxide synthase (iNOS) in hindlimb collateral tissue (229±47% of sedentary controls, p<0.01) and in mononuclear cells of the blood (2387±572%, p=0.025 for IL-6 expression, 72±6% in placebo-treated mice after 7 days, which was comparable to the sedentary group). Also, peri-collateral macrophage accumulation and up-regulation of iNOS were inhibited. NO-deficient mice did not show the exercise-induced perfusion restoration. Transplantation of bone marrow-derived mononuclear cells from NO-deficient mice into wildtype (WT) animals inhibited exercise-induced collateral artery growth (28.4±2.8% of non-ligated hindlimbs [iNOS−/− into WT] versus 57.4±4.2% [WT into WT]), (p<0.001).

Results: PAI1 co-localizes with arterial ligation increases the speed of perfusion restoration and enhances mononuclear iNOS expression. The perfusion increase is delayed by macrophage depletion. These data reveal that, in addition to a beneficial effect on vascular endothelium, physical exercise improves post-ischemic arteriogenesis through monocyte/macrophage related mechanisms.
days. Histology was performed on hind limb muscles to assess inflammatory cell influx (T cells and macrophages in peri vascular space) and collateral vessel geometry and numbers. To validate the results from Cd200−/− mice, wildtype (C57Bl/6J) mice were treated with a specific CD200R agonist after surgery, followed by laser-Doppler analysis and histological analysis.

**Results:** Cd200−/− mice had an increased perfusion recovery compared to wildtype (Cd200+/+ vs wildtype; 39%±3.3 vs 24%±3.0 %; p=0.002 at day 3; 59%±3.7 versus 53%±6.6; p=0.10 at day 7), accompanied by increased vessel geometry in the non ischemic muscle at seven days (P<0.05). Histology also revealed a significant increase in T cell influx (Cd200−/− vs wildtype; 4.3±0.8 vs 1.6±0.3; P<0.01 at day 3; 3.8±0.5 vs 1.9±0.3; P=0.01 at day 7). Cd200R agonist treatment resulted in a significant inhibition of perfusion recovery at day 7 (Cd200R vs IgG; 56%±0.9 vs 6.4±0.3; P<0.05 at day 7; 73%±1.0 vs 3.7±0.2; p=0.01 at day 7). In conclusion, collateral vessel geometry was lower (P<0.05) as well as influx of T cells (Cd200R vs IgG; 6.4±0.9 vs 3.6±0.6; p=0.03).

**Conclusions:** This study confirms the causal role of CD200-CD200R inhibitory signaling results in enhanced perfusion recovery, accompanied by increased collateral vessel growth and local T cell recruitment. These data were confirmed by triggering the Cd200R in vivo, resulting in opposite effects.

**2155 | BENCH**

**The APJ receptor: involvement in PECAM-1 induced mechanotransduction**

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**Aim:** Application of fluid shear stress to endothelial cells (ECs) elicits not only the induction of PECAM-1 (CD31) but also PECAM-1-signalings but also APJ receptor (APJ) signaling. These results lead us to the assumption, that similar effect these drugs on PWV, LV mass and blood pressure suggesting a direct effect of ACE on myocardial function.

**Methods:** HUVEC were transfected with specific APJ siRNA and transduced with adenoviral vectors for F-actin and APJ. Subsequently, we applied physiological stimulation of NO via PECAM-1 signaling to WT and APJ-deficient (APJ−/−) HUVEC using ibidi® slides. To determine interactions of APJ and PECAM-1, HUVEC were fixed and stained for PECAM-1 after shear stress exposure, and analyzed using confocal laser scanning microscopy (CLSM). Furthermore, WT and APJ−/− HUVEC were subjected to Atomic Force Microscopy (AFM). Cell-stiffness was analyzed using the Hertz-Model (HM) to calculate the Young’s Modulus (YM).

**Results:** To show an association of APJ and PECAM-1, we determined the Man- ders’ coefficient under static and flow conditions via CLSM. We found a time-dependent association of APJ and PECAM-1 under shear stress only (P<0.05). In APJ−/− ECs we also found a loss of cell-cell contacts accompanied by a loss of flow-induced eNOS (P<0.01) and PECAM-1 (P<0.01) mRNA expression leading to a decreased NO-release. PECAM-1 is also known to play a role in adaptive stiffening of ECs subjected to mechanical forces. Therefore, we determined the interaction of APJ on the elasticity of ECs. In accordance with the literature our AFM data show a stiffness-increase of 85% (P<0.05) in WT HUVEC after onset of flow. Interestingly, for flow-exposed WT HUVEC we found significantly higher YM-values of about 195% (p<0.01) compared to flow-exposed APJ−/− cells. In conclusion, stiffness measurements we also observed an flow-induced reorganization of actin-cytoskeleton structures in WT ECs using live cell imaging, which was impaired by APJ-silencing.

**Conclusion:** In HUVEC, shear stress elicits signals through PI3K/Akt/ENOS signaling resulting in an increase in NO-production, which might be related to a mechanically induced association of APJ and PECAM-1. Additionally, APJ-silencing results in a loss of cell-cell contacts, changes in morphology, and a loss of adaptive stiffening in response to the mechanical force. These results lead us to the assumption, that the APJ receptor is sufficient for PECAM-1-dependent responses to fluid flow.

**MULTIMODALITY APPROACH TO THE HYPERTROPHIC VENTRICLE**

**2160 | BEDSIDE**

**Angiogenesis converting enzyme inhibitors improve longitudinal myocardial deformation markers in patients with hypertension assessed by a novel one-beat real-time 3-dimensional speckle echocardiography**

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**Purpose:** Left ventricular (LV) systolic and diastolic properties in patients with hypertension assessed by a novel one-beat real-time 3-dimensional speckle echocardiography

**Methods:** We examined 41 patients with HTN without LV hypertrophy (41.0±11.4 years) with essential hypertension (age: 69.5±10.3) and isovolumetric relaxation (IVRT) using the novel 3D-STE. LV contractility and relaxation was assessed by strain rate (SR) during systole and isovolumetric relaxation (IVRT) using the novel 3D-STE. SR was calculated as LV stress / strain. Pulmonary capillary wedge pressure (PCWP) was estimated as 12.4±1.7 x log left atrial (LA) active emptying function/minimum LAV as we reported. LV stress was calculated as LV systolic or diastolic radius x systolic blood pressure (BP) or PCWP/LV end systolic or diastolic thickness (Th). LV strain was calculated as (end systolic Th - end diastolic Th)/end systolic Th.

**Results:** LV radial SR at systole and IVR were reduced in HTN. LV stiffness was increased in HTN with LVH associated with increase of LV diastolic stiffness compared with control and HTN without LVH (Table, *p<0.05 vs. control, +p<0.05 vs. LTN without LVH).

**Conclusion:** LV contractility and relaxation in HTN was reduced compared with control with no difference among 3 groups. Although LV stiffness in HTN without hypertrophy was comparable to control, LV stiffness in HTN with hypertrophy was increased. LV properties and feature in HTN could be noninvasively assessed by the novel 3D-STE.
On CMR study, left atrial volume (LAV) was 99.9 ml studied. significantly associated with the presence of severe renal impairment, defined by multivariable adjustment only the systolic time intervals (the IVCT (p=0.042) and the MPI (p=0.029)), remained significantly associated with the presence of hypertension. Furthermore, after multivariable adjustment only the systolic time intervals (IVRT/ET (p=0.002) and the myocardial performance index (MPI=(IVRT+IVCT)/ET)) were calculated.

Results: The cardiac time intervals revealed impaired systolic and diastolic cardiac function in participants with hypertension (n=613; IVRT (Mean±SD): 108±24 ms, p<0.001; IVCT: 39±15 ms, p<0.001; ET: 280±29 ms, p<0.001; IVRT/ET: 0.39±0.11, p<0.001; IVCT/ET: 0.14±0.06, p<0.001; MPI: 0.53±0.15, p<0.001) and remained significantly impaired by echoGFR (<60 ml/min/1.73m²) (IVRT: 108±24 ms, p<0.001; IVCT: 40±17 ms, p<0.001; ET: 289±27 ms, p<0.026; IVRT/ET: 0.38±0.09, p<0.001; IVCT/ET: 0.14±0.06, p<0.001; MPI: 0.52±0.12, p<0.001), compared to controls (n=898; IVRT: 93±20 ms; IVCT: 55±12 ms; ET: 286±23 ms; IVRT/ET: 0.33±0.08; IVCT/ET: 0.14±0.06; MPI: 0.53±0.15, p<0.001), after adjustment for age, gender, BMI, echoGFR, Heart Rate, diabetes, cholesterol, smoking status, atrial fibrillation, previous ischemic heart disease, previous ischemic stroke and conventional echocardiography (LVEF, LA dimension, LVMI, E/e', LV diastolic filling pattern and E/A-ratio) only the diastolic time interval (IVRT (p<0.001)) and the combined indexes, including information on both the systolic and diastolic performance (the IVRT/ET (p<0.002) and the MPI (p=0.029)), remained significantly associated with the presence of hypertension. Furthermore, after multivariable adjustment only the systolic time intervals (the IVCT (p=0.042) and the IVCT/ET (p=0.032)) and the combined index (the MPI (p=0.036)) remained significantly associated with the presence of severe renal impairment, defined by echoGFR <60 ml/min/1.73 m².

Conclusion: In the general population, persons with hypertension and reduced renal function have impaired cardiac function determined by the cardiac time intervals independently of the results of conventional echocardiography.

2163 | BEDSIDE

Increased left atrium volume but not fibrosis predicts long-term outcome in hypertrophic cardiomyopathy. A magnetic resonance study

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Background: It has been suggested that increased left atrial (LA) dimension and LA volume determined by transthoracic echocardiogram is associated with worse outcomes in HCM. CMR can measure precisely LA volume without limitations of echocardiography. We sought to determine the prognostic impact of LA volume determined by CMR in HCM patients.

Methods: We retrospectively studied all HCM patients undergoing CMR at 5 centers during the period 2006-2012. CMR findings were analyzed in relation to the appearance of a major adverse clinical event (heart failure requiring hospitalization, appropriate ICD discharge, aborted SCD and cardiovascular death) during follow-up.

Results: 399 patients (69% male, mean age 53±6 years, NYHA I 57%, LVEF 68±11%, maximum wall thickness 19±4 mm, 29% with LVOT obstruction) were studied. On CMR study, left atrial volume (LAV) was 99.9±37.6 ml and LAV indexed by body surface area (LAV/BSA) was 54±20.7 ml/m². After administration of gadolinium, 32% patients had fibrosis and 20% had extensive fibrosis (>3 segments). During a follow-up period of 38±24 months, 40 patients (10%) presented 45 clinical events (32 heart failure requiring hospital admission, 4 cardiovascular deaths, 3 aborted SCD and 6 appropriate ICD discharges). Patients with adverse events showed higher LAV and LAV/BSA (131.6±49.7 vs 96.5±34.4 cm³ and 74.6±30.3 vs 51.8±18.2 cm³/m²; both p<0.01). Other markers of poor prognosis on CMR were lower LVEF (59±16 vs 68±11%; p<0.01) and increased LV end-diastolic diameter (45±5 vs 39±4 mm; p=0.03). In contrast, the presence of fibrosis/extensive fibrosis was not associated with adverse events during follow-up (10% vs 9%; p=0.78 and 13% vs 9%; p=0.27, respectively.

A LAV cut-off value of ~96.5 cm³ predicted events with 80% sensitivity and 63% specificity and a LAV/BSA >62.1 cm²/m² with a 67% sensitivity and 79% specificity.

Conclusions: Increased left atrial volume is a marker of major clinical events among HCM patients. Our data suggest that enlarged LAV is a better marker than fibrosis for diastolic dysfunction and increased LV end-diastolic pressure in HCM patients.
difference excluded zero. Results are reported for Europeans (E), Asians (A) & South Asians (SA) of any weight.

Results: Of 13378 healthy subjects from 32 studies, there were: 4021 E, 564 A, 572 SA men; 4668 E, 570 A, 569 SA women. The slope of ln for E men was 1.7 which was significantly different to the slopes for A (1.1) or SA (0.8). For women, the slope of ln for E was 1.1 which was not different to A (1.1) or SA (0.6). The slope of BSA for E men was 1.3, which was significantly different to the slopes found for A (0.8) and SA (1.0). For women, the slope of BSA was 1.2 for E, which was not different to A (1.1) or SA (1.3) (Fig. 1).

Conclusions: Sex- and ethnic-specific indexation of LVM is indicated. Indexation of LVM by BMI was not appropriate for E men however this cannot be applied across other ethnicities, or to women. Similarly, indexation of LVM by BSA would be appropriate for E men but not A or SA men. Ethnic differences in indexation are less apparent among women.

BASIC AND TRANSLATIONAL SCIENCE HOT LINE ON CARDIAC DISEASE

2170
Modelling Brugada syndrome using patient-specific induced pluripotent stem cells

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Brugada syndrome (BrS), a cardiac genetic disease, is one of the major causes of sudden cardiac death in healthy young people. However, the underlying electro-physiological and molecular mechanisms have not been completely understood. A major challenge in translational research is the lack of tissue culture systems replicating human pathology to study disease mechanisms and to identify druggable targets. Aim of this study was to study the pathophysiology and molecular mechanisms of BrS in vitro using patient-specific induced pluripotent stem cells (iPSCs) as a renewable and unlimited source for cardiomyocytes (CMs). In this study, iPSCs were generated from a 45-year-old healthy donor and a 50-year-old patient with BrS by putatively cultured by the heterozygous point mutation C5435A in the gene SCN5A coding for the α-subunit of the cardiac sodium channel (Nav1.5). The generated iPSCs showed pluripotency and were able to differentiate into spontaneously beating CMs. Voltage-gated sodium current (INa) measurements revealed a significantly reduced current with a delayed activation in BrS-CMs compared to control cells, indicating a loss of function of Nav1.5. In BrS-CMs, the intermediate inactivation of sodium channels was slightly but not significantly enhanced whereas steady-state inactivation, recovery from inactivation, and persistent INa were not affected. Action potential (AP) measurements showed a reduced Vmax and higher arhythmic tendencies in BrS-CMs compared to control cells. A significantly higher variability of the AP durations as well as early and delayed afterdepolarizations could be observed. AP measurements in control cells under the treatment with the sodium channel blocker flecainide suggest that the increased variability of action potential duration in BrS-CMs is linked to the reduced INa. However, treatment of BrS-CMs with quinidine, a class 1 antiarrhythmic agent which is currently investigated for its therapeutic effect on BrS, could not reverse neither the voltage nor the variability of AP durations. Furthermore, a whole-cell real-time PCR showed that SCN5A was slightly but not significantly upregulated in BrS-CMs compared to the control cells with an allele-specific balanced expression. However, the full-length Nav1.5 protein was detected in BrS-CMs at a level comparable to control cells. These data demonstrate that patient-specific iPSCs can be used to model BrS in vitro and may provide the platform for the development of personalized drug therapy.

2171
Transplantation of adipose tissue mesenchymal cells conjugated with PLGA microspheres foster c-kit+ progenitor cells and cardiac regeneration through paracrine signaling

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Rationale: Adipose tissue-derived mesenchymal stem cells (AT-MSCs) may support cardiac repair after myocardial infarction. The engraftment and survival of transplanted stem cells in the heart and revascularisation of host myocardium may be improved by combining such cells with scaffolds to delay apoptosis and enhance their regenerative properties.

Objectives: We examined whether poly (lactide-co-glycolide) (PLGA) microspheres (PAM) functionalized with vascular endothelial growth factor (VEGF) enhance survival, growth and differentiation of AT-MSCs. We also compared the therapeutic efficacy of transplanted AT-MSCs conjugated with VEGF microspheres with injection of conditioned medium from AT-MSCs in a murine model of acute myocardial infarction (AMI).

Methods: We used non-functionalized (empty) or VEGF-releasing microspheres coated with murine AT-MSCs. Twelve month-old male C57BL/6 mice underwent coronary artery ligation (Lig), followed by randomization into 6 groups (n=5/group): I. Sham operation, II. AMI control (saline PBS 20 μL), III. AMI followed by intramyocardial injection with AT-MSCs only (2.5x10^5 cells/20 μL), or IV. Concentrated medium from AT-MSCs (CM, 20 μL), or V. AT-MSCs (2.5x10^5 cells/20 μL) conjugated with empty microspheres (V) or VI. VEGF-releasing microspheres (VI).

Results: Growth-curve and differentiation assays showed that VEGF-releasing microspheres did not impact proliferation or osteogenic and adipogenic differentiation of AT-MSCs. Conversely, AT-MSCs conjugated with VEGF-releasing microspheres inhibited H2O2-induced apoptosis, and this effect was dependent on the VEGF/Akt axis, since reverted by pre-incubation with the Akt inhibitor LY294002 or an anti-VEGF receptor antibody. In a Matrigel assay, AT-MSCs conjugated with VEGF-releasing microspheres were more pro-angiogenic than AT-MSCs alone. When compared with AT-MSCs alone, AT-MSCs conjugated with VEGF-releasing microspheres decreased the area of fibrosis and increased myogenic marker expression, arteriogenesis (Fig. 1A, immunofluorescence staining with anti-alpha smooth muscle actin conjugated with Cy3 red fluorochrome (Cy3-ASMA), number of cardiac-resident c-Kit positive cells (Fig. 1B, p<0.05 vs PBS-iig) and myocardial fractional shortening (FS) when transplanted into the infarcted hearts of C57 mice (%FS: I. 40±11, II. 15±3*, III. 29±7*, IV. 33±7*, V. 20±1, VI. 34±7*) (**p<0.01 vs sham; *p<0.05 and **p<0.01 vs Lig+PBS, anova test). All such effects, however, were fully paralyzed by the injection of CM (p<0.01 vs PBS-iig).

Conclusions: AT-MSCs conjugated with VEGF-releasing microspheres exert a paracrine effect, paralleled by the injection of CM, that may have therapeutic applications to enhance arteriogenesis, survival of AT-MSCs and the endogenous regenerative capacity of the heart. Such effects improve left ventricular function after AMI.
2173 Prediction of acute rejection in heart recipients: interest of circulating miRNAs

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Purpose of the study: Histological assessment of endomyocardial biopsies is the gold standard for diagnosis of acute rejection. However, the sampling procedure is invasive, sometimes associated with severe side effects, and pathologists’ appreciations are disparate due to the absence of a clear consensus, especially concerning AMR. Therefore, new biomarkers could both ease diagnosis on biopsy and correlate to early diagnosis on the tissue and serum expression of the disease. miRNAs are endogenous, single-stranded molecules that may represess target genes through degradation of the miRNA and/or inhibition of protein expression. miRNAs have been largely studied, especially in cancer, and their deregulation have been shown to be linked to many diseases, upon which diabetes, infecties, ischemia lesions or atherosclerosis. Here, we studied 14 miRNAs expression in a cohort of 100 patients, recipients having frozen endomyocardiacal biopsies samples and concomittant serum. These miRNAs were chosen from an in silico analysis conjugating relevant bibliography analysis and databases screening (TargetScan, MiRBase).

Methods: Samples from 100 patients, harvested and frozen in two centres (HEGP and La Pitie Salpetriere Hospital) were used. All biopsies were seen by trained pathologists and graded in term of rejection: 50 patients presented no rejection (GC, pAVD:n=19), 5 presented ACR (1R-3R) and 31 presented AMR mixed rejection (pAMR1-3, 1R-2R) (rejection group, n=50). Total RNA was extracted from the tissue and/or the serum and qPCR analysis was conducted. In parallel, DSA was assessed using Luminex technique. In situ hybridization was also conducted using paraffin-embed biopsies from patients presenting severe AMR and/or ACR.

Results: Six miRNAs showed a significantly different tissue expression during rejection (p<0.01): inflammatory miR-155 and 451, endothelial miR-10a and 92a, cardiac miR-21 and 31. All of these 6 miRNAs discriminated AMR from controls (p<0.01) while miR-155, miR-451, miR-10a, and miR-31 differentiated AMR from controls (p<0.03). Three miRNAs (miR-451, miR-10a, and miR-21) were able to discriminate ACVR and AMR (p<0.05). We demonstrate significant association (spearman correlation) between the tissue and serum expressions for miR-155 (p<0.0001), miR-10a (p=0.0002), miR-92a (p=0.0317) and miR-31 (p=0.0212). In situ hybridization for miR-92a showed an endothelial distribution, whereas 10a was also present in inflammatory cells and 31 was mostly found in interstitial cells.

Conclusion: This study provides evidence that regulation in the expression of miRNA occurs during heart rejection, not only at the tissue level in the EMB but also in the concomitant serum. This suggests that miRNA may represent interesting biomarkers for better investigating heart transplant rejection.

2175 A mutation in elongator protein 2 can cause a severe form of familial hypertrophic cardiomyopathy

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Background: Elongator protein 2 (ELP2) is known as a STAT3-interacting protein and one of subunits of elongator, which can regulate RNA elongation via its histone acetyltransferase activity. It remains to be solved whether ELP2 plays an important role in cardiac hypertrophy.

Purpose: Our purpose is to identify new gene mutations that cause familial HCM, and the role of ELP2, which is also known to be involved in familial HCM.

Methods: We examined a patient and her elder brother who both presented with complicated severe HCM and whose parents were married cousins. The elder brother had died suddenly as a boy; his autopsy revealed that he had developed HCM. The patient was diagnosed with HCM, and during the 20-year follow-up, HCM progressed to d-HCM. The patient received a left ventricular-assist device implant, and the patient is currently on a waiting list for cardiac transplantation.

Results: ELP2 mutation was found in the patient and his elder brother, which affects a missense mutation (p.A408VfsX12) in ELP2. The patient and her elder brother were compound heterozygotes in ELP2, which was inherited from both parents. Both parents were heterozygous. The patient was also found to have familial HCM, and the patient’s parents were consanguineous. The patient developed severe HCM with cardiac hypertrophy, and d-HCM during the 20-year follow-up. The patient’s elder brother died at an early age, and the patient presented with progressive course of HCM.

Conclusion: ELP2 mutation is a potential cause of familial HCM, and ELP2 gene is a potential therapeutic target for familial HCM.
oral anticoagulation (OAC) is highly effective at preventing stroke and mortality in non-valvular atrial fibrillation (NVAF) patients. However, the efficacy and safety of vitamin K antagonists (VKAs, the main OAC drug used) strongly depend on the quality of anticoagulation control, as reflected by the average percentage of the time in therapeutic range (TTR) of INR 2.0-3.0. An easy, simple prediction of which AF patients are likely to do well on VKA (with good average TTR) could guide decision-making between using VKAs and novel OACs. Recently, it has been proposed and validated the SAME-TT2R2 score (Sex, Age <60 years), Medical history (at least 2 of the following: hypertension, diabetes, coronary artery disease/myocardial infarction, peripheral arterial disease, congestive heart failure, previous stroke, pulmonary disease, hepatic or renal disease), Treatment (interacting drugs) [all 1 point], as well as current tobacco use [0.001], and all-cause mortality [1.41 (1.16-1.67); p<0.001]. Patients with increasing baseline SAME-TT2R2 score had significantly lower mean TTR at 6 months after inclusion (p=0.043).

Conclusion: In a “real world” cohort of consecutive patients with NVAF, a high SAME-TT2R2 score (reflecting poor anticoagulation control with poor TTR) was associated with more bleeding, adverse cardiovascular events and mortality during follow-up. 

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Anticoagulation therapy “the times they are a changing” / New and unique: treatment of structural heart disease 383

2189 | BEDSIDE
Comparison of estimated glomerular filtration rate equations for dosing new oral anticoagulants in patients with atrial fibrillation
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Background: New oral anticoagulants (NOAC) require dosing adjustment according to renal function status. The aim of this study was to determine the discordance in hypothetically recommended dosing of NOAC using kidney function estimates based on different estimated Glomerular Filtration Rate (GFR) equations in patients with atrial fibrillation (AF).

Methods: Cross-sectional analysis of 910 consecutive patients with AF and indication for oral anticoagulation from our outpatient anticoagulation clinic. GFR was estimated by using the following equations: Cockcroft-Gault (CG), Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). For dabigatran, rivaroxaban and apixaban, we identified dose discordance when there was a disagreement in recommended dose based on two different GFR estimates.

Results: Among the overall population, relative to CG the discordance in dabigatran dosage was 11.4% for MDRD and 10% for CKD-EPI, whereas the discordance in rivaroxaban dosage was 11.4% for MDRD and 10% for CKD-EPI. In patients with CG <60 mL/min or in the elderly (>75 years), the discordance in dabigatran and rivaroxaban dosages were higher than in the whole population, ranging from 13.2% to 30.4%. The discordance in apixaban dosage remained <5% in these patients.

Conclusions: In this population, the discordance in dabigatran and rivaroxaban dosages using different estimated GFR is frequent, especially among the elderly patients with renal impairment. Further studies are needed to clarify the clinical importance of these discrepancies and the best anticoagulant dosages depending on the use of different estimates estimated GFR.

2190 | BEDSIDE
Left atrial thrombi and spontaneous echo contrast in patients with atrial fibrillation who were taking warfarin or novel oral anticoagulants before cardioversion
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Introduction: Warfarin reduces the risk of stroke and systemic embolism following cardioversion in patients with atrial fibrillation. It was reported that the novel oral anticoagulants (NOAC) have similar efficacy compared with warfarin. But the data of left atrial thrombus before cardioversion was limited in these patients.

Methods: Total 170 patients [102 patients in warfarin group, 68 patients in novel oral anticoagulant group (40 in dabigatran, 28 in rivaroxaban)] undergoing transcatheter echocardiography before cardioversion were included. The presence of left atrial thrombus or spontaneous echo contrast was investigated.

Results: Baseline characteristics were similar between groups. Among 170 patients, there was no thrombus in left atrium. Positive rate of spontaneous echo contrast in transesophageal echocardiography was 25.5% in warfarin group and 30.9% in novel oral anticoagulant group (P=0.441). Continuous treatment with anticoagulants for 3 weeks before cardioversion was 95.1% in warfarin group and 89.7% in novel oral anticoagulant group (P=0.225). At 30 days after cardioversion, the incidence of stroke was 2.0%, 1.5%, respectively (P=0.999).

Conclusion: The incidence of thrombus and spontaneous echo contrast in patients with atrial fibrillation receiving anticoagulants was not different in warfarin and novel oral anticoagulant group. Also the incidence of stroke and systemic embolism after cardioversion was not different in two groups.

NEW AND UNIQUE: TREATMENT OF STRUCTURAL HEART DISEASE

2211 | BEDSIDE
Percutaneous transcatheter obliteration of mitral paravalvular leaks
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Introduction: Prosthetic paravalvular leaks (PVL) of biological or mechanical heart valves implanted surgically are sometimes responsible of heart failure or hemolysis requiring reoperations, which are often of high risk. The percutaneous occlusion of these leaks is an alternative treatment. The aim is to assess the feasibility and efficacy of percutaneous transcatheter obliteration of paravalvular leaks.

Methods: Fourteen patients underwent transcatheter closure of prosthetic mitral paravalvular leaks from September 2009 to December 2013 in one center. All patients had symptoms and signs of hemolysis and/or severe cardiac failure with high surgical risk. Each percutaneous transcatheter intervention was guided by three dimensions trans-esophageal echocardiography (3D TOE) and performed with different kinds of Amplatzer devices.

Results: Patients had high operative risk (average logistic EuroSCORE 1 = 18.1%) mainly because of previous cardiac surgeries (3 times in 4 patients, 2 times in 8 patients and 1 time in 2 patients) and comorbidities. Implantation of a device was impossible in 4 patients without any complication. Implantation of a device has been technically successful in 10 patients (71.5%): out of them, 7 underwent mitral implant directly and remained asymptomatic on the follow up. In the 3 other patients, 1 had an immediate migration of the prosthesis into the left atrium without consequence, 1 had few months after 2 occasions enlarged the leak in spite of 2 new successful implantations of prosthesis and finally died of heart failure, 1 patient had a severe complication with a dramatic worsening of the hemolysis on a residual leak leading to death in spite of the full occlusion of the residual leak with a second device.

Conclusions: Transcatheter closure of paravalvular leaks is technically feasible and facilitated by the 3D TEO and the provision of new devices. Despite the difficult implantation, this technique represents an attractive alternative to surgery in these high risks patients.

2212 | BEDSIDE
Transcatheter closure of large patient ductus arterioles with the self-expanding mushroom-shaped duct occluder
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Purpose: To assess the immediate, short, and intermediate-term results of transcatheter closure the large patent ductus arteriosus (PDA) with the self-expanding mushroom-shaped duct occluder (DO) from a single center.

Methods: Between March 2008 and December 2012, 318 patients underwent attempted transcatheter closure of PDA in our center, of whom DO was used in 73 (23%) patients with large-sized PDA (71 female, with ages ranging from 17 to 73 years). Large PDA is defined as ductus diameter >5 mm. The size of device selected was generally at least 1.2 mm larger that ductus diameter. 49 (67%) patients were symptomatic. 8 (11%) patients were in severe heart failure. Six patients had successful closure PDA by using ventricular septal defect occluder. A hemodynamic study was performed and the Qp/Qs ratio was calculated in each patient. Ten minutes after detachment of device, an aortogram was performed to check the presence of residual shunt and aortic arch obstruction.

Results: The ductus diameter ranged from 6.2 to 12 mm (mean 8.9±1.4 mm). The mean Qp/Qs ration was 2.7±0.7. Pulmonary arterial hypertension (pulmonary arterial systolic pressure >40 mm Hg) was present in 43 (59%) patients. There were 59 patients with morphological type A ductus, 3 with type B ductus, 9 type C ductus and 2 type E ductus. DO was successfully deployed in all patients. The size of device deployed ranged from 8 to 14 mm. 1 patient experienced severe hemolysis and major bleeding was analyzed. Between March 2008 and December 2012, 318 patients underwent attempted transcatheter closure of large-sized PDA. Also the incidence of stroke and systemic embolism between warfarin group and novel oral anticoagulant group. However, none had residual fluid across the device in 24 hours after the procedure. Complete occlusion was documented by the echocardiography in all patients for 1-year follow-up. No patient had left pulmonary artery stenosis. Severe pulmonary arterial hypertension was in 9 (21%) of 43 patients at 1 year after a device implantation.

Conclusion: Transcatheter closure of large-sized ductus with DO is effective and safe.

2213 | BEDSIDE
Intraprocedural assessment of mitral valve area with 3D-TEE during percutaneous mitral valve repair
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Purpose: Percutaneous mitral valve repair with the Clip device can reduce mitral regurgitation by improving coaptation of the leaflet and will result in a reduction of effective mitral valve area. To prevent complications and achieve optimal clinical outcomes, intraprocedural monitoring for significant stenosis is mandatory. While transvalvular pressure gradients measured with continuous Doppler are used routinely, the value of 3D planimetry of the valve area has not been examined conclusively despite being recommended as the standard modality for native valve stenosis.

Methods: Echocardiographic intraprocedural data from 130 consecutive patients undergoing percutaneous mitral valve repair with the Clip device were analyzed. Mitral valve area was determined by planimetry of each individual orifice for 3D-TEE during percutaneous mitral valve repair with the Clip device can reduce mitral regurgitation by improving coaptation of the leaflet and will result in a reduction of effective mitral valve area. To prevent complications and achieve optimal clinical outcomes, intraprocedural monitoring for significant stenosis is mandatory. While transvalvular pressure gradients measured with continuous Doppler are used routinely, the value of 3D planimetry of the valve area has not been examined conclusively despite being recommended as the standard modality for native valve stenosis.

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Results: Of 130 patients had 88 had 1 Clip, 34 had 2 Clips, 3 Clips were implanted in 3 patients and 1 patient had 4 Clips implanted. Four patients had no Clip implanted after showing signs of significant stenosis with temporary clip placement. All 4 had 3D MVA <1.5 cm² with 3D planimetry. Of the remaining 126 Patients, 19 had mean Gradients above 5 mmHg at discharge or in follow-up. MVA analysis yielded MVA <2 cm² in 11 of 19 patients using the pressure half time method and in 14 of 19 using 3D planimetry. 20 Patients had an intraprocedural mean gradient of 5 mmHg or greater. 35% of these patients had gradients below 5 mmHg at discharge and in follow-up. The patients with low gradients after the procedure had higher heart rates (81 vs. 69 bpm), and mitral valve areas in both PHT-MVA (2.15 vs. 1.97 cm²) and 3D MVA (1.83 vs 1.77 cm²). After Clip-Implantation the residual mitral valve area measured during the procedure was 2.21±0.84 cm² with 3D planimetry (3D MVA) vs. 2.33±0.83 cm² for the pressure half time method (p=0.170). Intraprocedural mean gradients increased significantly from 2.86±1.63 mmHg to 3.68±1.82 mmHg at discharge (p<0.001) and then remained stable in follow up (3.48±1.87 mmHg; p=0.75). Conclusion: As Doppler gradients are influenced by heart rate and hemodynamic situation, 3D-planimetry can be helpful during PMVR to assess the probability of significant stenosis. Gradients at discharge are generally higher than during the procedure. When borderline doppler results are obtained or patients have bradycardia, 3D planimetry of the mitral valve area should therefore be considered as an alternative and possibly more sensitive method.

2214 | BEDSIDE
Left atrial decompression through left-to-right interatrial shunt for the treatment of left cardiac heart failure: first-in-man experience with the V-Wave device
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Methods: Two patients with left ventricular dysfunction and NYHA class III despite optimal treatment, pulmonary wedge >18mmHg and no right heart dysfunction were planned for FIM V-Wave experience.

Results: The patients were treated successfully. Left-to-right shunt was verified postprocedureally and at 3-month by TEE (Results in Table 1B).

Table 1B

<table>
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Conclusions: Decompression of LA through left-to-right shunt with the V-Wave device is feasible in humans. Complete results of the V-Wave FIM experience (5 patients) will be presented at the meeting.

2215 | BEDSIDE
2-year clinical outcome after left atrial appendage closure with the amplatzer cardiac plug device in patients with non-valvular atrial fibrillation and contraindications for anticoagulation therapy
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Introduction: Left atrial appendage (LAA) closure can be an attractive option for patients with non-valvular atrial fibrillation (NVAF) with contraindications to anticoagulants. The aim of this study is to observe the rate of stroke and bleeding events in a 2-year follow-up period after LAA closure with the Amplatzer Cardiac Plug device.

Methods: A multicenter retrospective registry was made of 167 consecutive patients after ACP implantation in 12 hospitals in Spain (10) and Portugal (2). Procedural success was in 158 patients (94.6%). The incidence of stroke and major bleeding events as well as echocardiographic findings were evaluated over a 2-year follow-up period after implantation.

Results: Mean age was 74.7±18.6 years. 61.1% were males. Median CHADS2 and HASBLED scores were 3 (2-4) and 3 (3-4). LAA closure indications were: gastrointestinal bleeding in 30.5%, intracranial hemorrhage in 22.8%, other hemorrhages in 16.8%, thromboembolic events under anticoagulant therapy in 7.2%, high-risk of bleeding in 4.2% and others in 19.2%. The observed 24-month rates of stroke and major bleeding events were 63% and 54% lower than expected according to CHADS2 and HASBLED scores (4.4 vs 12%; p=0.001 and 5.7 vs 12.5%; p=0.002).

Conclusion: Reductions in stroke and bleeding events after LAA closure become evident from the first year onwards. This could be explained by the formation of thrombi on the device in the first months in the case of stroke, and by the bleeding events more often during the first year, with a rate that is very similar to anticoagulant treatment in elderly patients.

2216 | BENCH
Treatment of severe mitral stenosis with percutaneous balloon commissurotomy in pregnant patients in a tertiary Tunisian center of cardiology
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Pregnancy can cause life-threatening complications in women with mitral stenosis. Frequently, there is an urgent need to increase the mitral valve area mechanically.

In selected cases, percutaneous mitral balloon commissurotomy (PMBC) has emerged as a safe and effective alternative to surgical commissurotomy.

Goal: To present our experience of PMBC in 16 pregnant patients with severe symptomatic mitral stenosis.

Methods: During 15 years, in our department, 379 PMBC were successfully performed in women, 16 of them pregnant at around 24 weeks of gestation. The patients were in New York Heart Association (NYHA) functional class III or IV who did not respond positively to drug treatment.

Results: Percutaneous mitral commissurotomy was performed in 16 pregnant females aged 33±5.03 years (range 23-38 years) with severe mitral stenosis at around 24 weeks of gestation. All patients were in New York Heart Association functional class III or IV at the time of procedure. After the procedure, all patients showed marked immediate clinical and hemodynamic improvement, NYHA functional class I-II. After dilatation, the mean left atrial pressure decreased from 28±6.53 to 13±4.85 mmHg (p=0.037), the mitral valve pressure gradient decreased from 21±5.88 to 7.5±5.34 mmHg (p=0.015) and the calculated mitral valve area increased from 1.0±0.18 to 2.0±0.37 cm². During the procedure, there were no maternal or fetal complications. All patients had uneventful term deliveries.

Conclusion: Percutaneous mitral balloon commissurotomy is a safe and effective procedure for selected pregnant patients with severe mitral stenosis who are refractory to medical treatment. Severe mitral regurgitation requiring immediate surgery may occur occasionally. The possible harmful effects to the fetus from its exposure to radiation during PMBC are unknown.
**2221 | BEDSIDE**  
**Purpose:** Selective pulmonary vasodilation in patients with pulmonary hypertension due to systolic LV dysfunction (PH-LVd) may result in adverse increases in PCWP when PVR is elevated. This exploratory post-hoc analysis of the LEPHT study compared the effects of the novel soluble guanylate cyclase stimulator, riociguat, in PH-LVd patients with PVR (>240 dyn s/cm²) at baseline.

**Methods:** 201 patients with systolic HF and mPAP ≥25 mmHg were randomized to riociguat (0.5, 1, or 2 mg tid) or placebo for 16 wks.

**Results:** Ischecnic ejection (57 ± 20%) and diabetes mellitus (51 ± 34%) were more frequent in patients with PVR > 240 dyn s/cm² at baseline; other baseline characteristics were well balanced between subgroups. At wk 16, riociguat 2 mg decreased SVR in patients with low PVR and high PVR at baseline (Table). Riociguat 2 mg was associated with a significant decrease in PCWP in the low PVR subgroup and no significant changes in PCWP in patients with high baseline PVR. Riociguat 2 mg also significantly increased stroke volume and pulmonary artery compliance (PAC), and improved MLHFI questionnaire score in the low PVR subgroup at Wk 16. The relationship between PAC and PVR showed a favorable shift in the low PVR subgroup.

**Conclusion:** Improvements in hemodynamics and QoL with riociguat were greater in PH-LVd patients with low baseline PVR than those with high baseline PVR.

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**2222 | SPOTLIGHT**  
Pro-atrial natriuretic peptide1-126: a novel guanylyl cyclase-A activator with selective renal enhancing and cardiac unloading properties which goes beyond carperitide and nesiritide

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**Purpose:** The atrial natriuretic peptide (ANP) precursor proANP1-126 is produced in the atria and processed to mature ANP1-28 (carperitide) which activates the guanylyl cyclase receptor-A (GC-A) and its second messenger cGMP. ProANP1-126 is found in the human circulation and we previously reported that proANP1-126 is activates GC-A in vitro and is processed into ANP1-28 in human cells. The aim of this study was to evaluate whether abnormalities in Renal Resistance Index (RRI), a parameter reflecting renal perfusion, are associated to changes in diuretic therapy in a group of chronic heart failure (CHF) outpatients.

We enrolled 188 outpatients (77% males, 65±14 years, NYHA class 2±3±0.6; left ventricular ejection fraction, LVEF, 34±10% with CHF, in stable clinical conditions (≤1 month), who were taking loop diuretics. Peak systolic velocity and end diastolic velocity of segmental renal artery was obtained by pulsed Doppler flow and RRI was then calculated. Furosemide equivalent dose was evaluated at baseline and after 1 year. During the study, it was prescribed the minimum furosemide dose able to keep patient in stable clinical conditions.

The mean diuretic dose increased from 71±7.1 to 85.1±104 mg/day and 35 patients (18%) needed an increase of diuretic dose >50%. Baseline diuretic dose was not different when groups with and without diuretic dose increase were compared (77.1±7.2 vs. 71±7.3 mg/die, p<0.03). At univariate regression analysis RRI was associated with 1 year increase >50% (p<0.001) and it remained significantly associated (p=0.042) in a multivariate model including the other univariate predictors, i.e. LVEF, peak of tricuspid annulus excursion, estimated central venous pressure, NT-proBNP and GFR-EPI. Figure 1 shows a RRI >71 was associated both to a significantly higher baseline diuretic dose and to its increase at 1 year.

In conclusion, our findings demonstrate that an altered RRI, which reflects abnormal renal perfusion, is associated both to higher baseline loop diuretic dose and to its significant increase over 1 year, thus suggesting its possible clinical usefulness in order to better detect patients prone to develop diuretic resistance.

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**2224 | BEDSIDE**  
**Purpose:** To compare clinical efficacy and safety of indacaterol and tiotropium administration in patients with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

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**Efficacy and safety of different types of bronchodilator therapy in patients with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease**


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Purpose: To compare clinical efficacy and safety of indacaterol and tiotropium administration in patients with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease.
and long-acting bronchodilator therapy in patients with CHF combined with COPD raises efficiency of treatment. The tiotropium and indacaterol inclusion in the structure of combination treatment significantly improved quality of life in MMRC dyspnea grade (22.1%, 25.2%, 28.5% respectively). All treatment options in 1st, 2nd and 3rd group LVEF was increased by 8.4%, 9.3% and 10.0%, respectively. Episodes of silent myocardial ischemia decreased by 15%, 16.9% and 21.9%, respectively. Towards the end of the observation period, in all groups there was a confident and authentic increase of forced expiratory volume during 6-min walk distance increased by 18.7%, 23.1% and 29.8% accordingly. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (16.6%, 20.4%, 25.0%) and MYHFQ score (27.9%, 24.9%, 32.0%), significant improvement in LVEF (40%, 45% and 50%). These findings from real-world clinical practice indicate that the effectiveness of carvedilol and metoprolol succinate in patients with heart failure (HF) is similar. Combination of these drugs significantly enhances the positive effects of the therapy.

2225 | BEDSIDE

Carvedilol vs. metoprolol succinate and risk of mortality in patients with heart failure: national cohort study

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Purpose: Carvedilol and metoprolol succinate both reduce mortality in patients with heart failure (HF), but the comparative clinical effectiveness of these drugs is unknown. We tested the hypothesis that carvedilol is superior to metoprolol succinate.

Methods: From a Danish national HF registry linked with health care and administrative databases, we identified a cohort of patients with incident HF with reduced left ventricular ejection fraction (LVEF < 40%), who received carvedilol (n=2631), metoprolol succinate (n=5295), carvedilol (n=5295), metoprolol succinate (n=5295), and carvedilol (n=5295). Overall, 4326 patients were included in the analysis. Patients with a history of ischemic heart disease, HF with preserved ejection fraction, HF with New York Heart Association (NYHA) class IV, and HF due to other causes (such as valvular disease) were excluded.

Results: After 6 months of therapy the improvement of clinical condition and quality of life were marked in all groups. In 1st, 2nd and 3rd group LVEF was increased by 40%, 50%, and 60% respectively. The rates of AKI were comparable (22% and 23%). The hospital length of stay was shorter with carvedilol (35% vs. 23% p=0.02), and the hospital mortality was lower in the carvedilol group (6.6% vs. 0.3% p<0.01), and SGRQ and mMRC.

Conclusions: The tiotropium and indacaterol inclusion in the structure of combination treatment improves quality of life, basic parameters of central hemodynamics and pulmonary function. Efficacy of long-acting inhaled anticholinergic agent (tiotropium) and long-acting β-agonist (indacaterol) in patient with CHF due to CAD combined with COPD are similar. Combination of these drugs significantly enhances the positive effects of the therapy.

2226 | BEDSIDE

Continuous versus bolus intermittent loop diuretic infusion in acutely decompensated heart failure: a prospective randomized trial

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Purpose: Intravenous loop diuretics are a cornerstone of therapy in acutely decompensated heart failure (ADHF). We sought to determine if there are any differences in clinical outcomes between intravenous bolus and continuous infusion loop diuretics.

Methods: Subjects with ADHF within 12 hours of hospital admission were randomly assigned to continuous infusion or twice daily bolus therapy with furosemide. There were 3 co-primary endpoints assessed from admission to discharge: the mean paired changes in serum creatinine and estimated glomerular filtration rate (eGFR), and reduction in B-type natriuretic peptide (BNP). Secondary endpoints included the rate of acute kidney injury (AKI) change in body weight and six months follow-up evaluation after discharge.

Results: A total of 43 received a continuous infusion and 39 were assigned to twice daily bolus therapy. At discharge, the mean change in serum creatinine was higher (0.08±0.4 vs. -0.03±0.3 mg/dl p<0.01), and eGFR was lower (-9.7±5 vs. +5.6±1.7 ml/min/1.73m² p<0.05) in the continuous infusion group. There was no significant difference in the degree of weight loss (-4.1±1.9 vs -3.5±2.4 kg p=0.23). The continuous infusion arm had a greater reduction in BNP over the hospital course, (-767±655 vs. -181±527 pg/ml p=0.02). The rates of AKI were comparable (22% and 15% p=0.3) between the two groups. There was more frequent use of hypertonic saline solutions for hypotension (33% vs. 18% p<0.01), intravenous dopamine infusions (35% vs. 23% p=0.02), and the hospital length of stay was longer in the continuous infusion group (14.3±5 vs. 11.5±4 days p=0.03). At 6 months there were higher rates of re-admission or death in the continuous infusion group, 58% versus 23% (p=0.001) and this mode of treatment independently associated with this outcome after adjusting for baseline and intermediate variables (adjusted hazard ratio=2.57, 95% confidence interval, 1.01-6.58 p=0.04).

Conclusions: In the setting of ADHF, continuous infusion of loop diuretics resulted in greater reductions in BNP from admission to discharge, however, this appeared to occur at the consequence of worsened renal filtration function, use of additional treatment, and higher rates of rehospitalization or death at six months.
Akt were similarly activated in MK118 and in PostC groups but not in controls. MK118 and PostC also caused similar phosphorylation of GSK3β and STAT3.

**Conclusion:** MK118 significantly reduces infarct size compared to PostC. This cardioprotective effect is related to Akt and STAT3 activation, as well as GSK3β inhibition and is independent of NO release, endogenous NO production and adenosine receptor activation.

### 2236 | BENCH

**Phospholamban is a final effector of ischaemic postconditioning and H2S induced cardioprotection**


**Purpose:** As phospholamban (PLN) regulates cytosolic Ca2+ levels, we sought to explore the role of PLN in ischaemic PostC.

**Methods:** Twenty three wild type Sv129J and twenty one PLN(−/−) homozygous knockout mice of both sexes were subjected to 30 minutes regional ischemia (isc) followed by 40 minutes reperfusion. No significant differences were detected in the (R) among the studied groups.

**Results:** Control wild type had similar normoxic control animals (42.1±2.6% vs 38.0±2.9%, p=NS). Wild type animals, PostC application and NaHS administration conferred a significant benefit compared to control (14.9±2.1% and 15.5±1.2% respectively vs 42.1±2.6%, p<0.05). However, neither PostC nor NaHS conferred cardioprotection in PLN(−/−) animals (45.2±2.1% and 42.2±1.5% respectively, p<0.05 vs wild type PostC and NaHS groups).

**Conclusion:** Our findings suggest that ischemic and pharmacological postconditioning induced by H2S administration requires PLN activation.

### 2237 | BENCH

**Concomitant therapy with vagal nerve stimulation (VNS) and total flow reperfusion reduces infarct size in ischemia reperfusion (IR) model**

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**Purpose:** Even the recent advances in the management of acute myocardial infarction cause the inevitable loss of myocardium, which impairs cardiac function and leads to worsening heart failure in the long term. It has been established that LVAD reduces the infarct size in IR model as well as VNS. In this study, we investigated how the combination of VNS with LVAD impacts on reducing the infarct size in IR dogs.

**Methods:** We allocated 17 anesthetized dogs into 4 groups, Control (n=5), VNS (n=4), LVAD (n=4) and VNS+LVAD (n=4). After a median sternotomy, we ligated the major branches of the left anterior descending coronary artery for 90 min and reperfusion thereafter for 300 min. We titrated the amplitude of VNS to lower heart rate by 10-20%. We set the LVAD flow to create a totally LVAD-dependent circulation where LV no longer ejection. We performed each treatment from the beginning of ischemia and assessed the infarct size (normalized by the risk area) at the end of the reperfusion.

**Results:** Mean aortic pressure did not differ among 4 groups (Control: 91.5±6.1, VNS: 95.1±12, LVAD: 102±7.0 and VNS+LVAD: 97±4.9mmHg). Left atrial pressure was much lower in LVAD and VNS+LVAD (Control: 13±1.7, VNS: 9.9±1.7, LVAD: -9.6±1.6, VNS+LVAD: 0.0±0.85mmHg, p<0.0001). VNS and LVAD significantly reduced the infarct size (Control: 44±2.4, VNS: 28±2.1 and LVAD: 5.0±1.6%, p<0.001), showing the % reduction relative to Control was 36% and 88%, respectively. VNS+LVAD further reduced and almost nullified the infarct size (0.55±0.55%, p<0.0001).

**Conclusion:** The combination therapy of VNS with total flow support LVAD maximally suppresses the infarct size in IR model without compromising hemodynamics. It could serve as a powerful therapeutic strategy to preclude post MI heart failure.

### 2238 | BENCH

**Administration of exogenous oxygen may worsen myocardial ischemia**

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**Purpose:** It has been demonstrated that hypoxemia has a vasodilating effect on coronary arteries. Although recent guidelines limit the use of excessive oxygen concentrations after cardiac arrest, the impact of hypoxemia on myocardial oxygenation is not well understood. Oxygenation-sensitive (OS) cardiovascular magnetic resonance (CMR) allows for monitoring gas-dependent changes in myocardial oxygenation.

**Methods:** An MRI-compatible flow probe was implanted on the proximal left anterior descending (LAD) coronary artery in 16 swine. In 8 animals an acute LAD stenosis was created with a hydraulic occluder. The severity of stenosis was assessed by measuring fractional flow reserve (FFR). Blood gases were set to physiologic levels (pO2=100mmHg, pCO2=40mmHg) and CMR images were acquired using a clinical MRI system (3T). Measurements were repeated after paO2 was increased to 300mmHg. OS-CMR images were analysed in end-systolic frames.

**Results:** Mean FFR across the induced stenoses was 0.63±0.02. During hyperoxemia, coronary blood flow was reduced by 14.8±4.4% (p<0.05) in the control animals and by 15.6±2.6% (p<0.01) in the animals with stenotic vessels. In OS-CMR images of animals without stenosis the +1.99±0.94% change in signal intensity (SI) did not differ from the remote myocardium. In animals with induced stenosis SI decreased by 3.20±2.23% in the LAD territory, as opposed to the increases in both the remote myocardium of the same animal (2.64±1.45%) and the LAD territory of the healthy group (p<0.05).

**Conclusion:** Hyperoxemia may lead to a net reduction of tissue oxygenation in myocardial segments with severe coronary artery stenosis. Therefore, in these patients, the administration of oxygen may have detrimental effects.
2240 | BENCH
Preserved cardioprotective effect of ischemic preconditioning during mild hypothermia in isolated rat hearts
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Purpose: Ischemic preconditioning (IPC) and mild hypothermia (MH) reduce cardiac ischemia-reperfusion (IR) injury. Because patients with cardiac arrest due to acute myocardial infarction benefit from MH, we aimed to investigate whether the cardioprotective effect of IPC is preserved during MH.
Methods: Isolated rat hearts perfused a.m. Langendorff underwent 40 min stabilization/40 min global ischemia/120min reperfusion at 37 °C. IPC was induced by two cycles of 5 min IR. MH (34°C) was induced during the whole ischemic period (MH-I), for the final 20 min of ischemia (MH-I20), during reperfusion (MH-R) or during the total study protocol (MH-T). The cardioprotective effect was evaluated by hemodynamic recovery and infarct size (IS). To evaluate potential mechanisms we analyzed intermediary metabolism by microdialysis.
Results: MH reduced IS (Fig. 1) and improved hemodynamic recovery compared to normothermic controls when applied during ischemia, but not when applied during reperfusion alone. Addition of IPC further reduced IS significantly in all MH protocols. Although IS was consistently lower in all protocols combining IPC with MH during ischemia, MH did not significantly reduce IS over and above IPC alone (MH-I: p=0.34, MH-I20: p=0.16, MH-R: 0.68, MH-T: p=0.07). During ischemia interstitial concentrations of lactate and purine metabolites were lowered by MH but not IPC.

Conclusion: The cardioprotective effect of IPC is preserved during MH and adds further protection to the cardioprotective effect of MH during ischemia. The additive cardioprotective effect and differences in metabolism during ischemia may reflect different cardioprotective targets by MH and IPC.

THE FUTURE IS NOW: CARDIOVASCULAR DISEASES IN THE ELDERLY

2249 | BEDSIDE
Centenarians and their heart: a prospective registry with comprehensive geriatric assessment, ECG, echocardiography, and follow-up
Background: Data on the cardiac characteristics of centenarians are scarce. Our hypothesis is that the heart of a centenarian shows typical age-related anatomical and physiological changes. The aim of this study was to describe ECG, echocardiography, and blood test results in a cohort of centenarians and to correlate them with survival and with clinical data obtained from the medical history and a comprehensive geriatric assessment.
Methods: Prospective multicenter registry of 118 centenarians (28 men and 90 women) with a mean age of 101.5±1.7 years.
Results: Normal ECG recordings were more frequent in women (31.3% vs. 8.7%, p=0.01). The mean duration of the PR interval was 195±43 ms. 27% (23%) presented atrial fibrillation or flutter, 15% had left and 9% right bundle branch block. Echocardiography was performed in 100 subjects (84.7%). Mean left ventricular (LV) dimensions were 4.0±0.7 cm (end-diastolic) and 2.6±0.7 cm (end-systolic). Mean LV ejection fraction was 50.0±10.3%. Mean LV posterior wall thickness was 1.1±0.19 cm. The most frequent valve disease was aortic regurgitation, which was present in 49% (36 mild, 11 moderate, and 2 severe). Moderate or severe valve aortic stenosis was found in 16% and mitral insufficiency in 15%. Diastolic dysfunction was assessed in 79 subjects, 55 of whom (69.9%) presented it. The variables independently associated with the ability to walk 6 m were nutritional assessment and LV dilatation. All subjects underwent a complete follow-up for at least 6 months. Independent predictors of mortality were age, aortic regurgitation, and the Charlson and Katz indexes.

Conclusions: Our results add to our knowledge of cardiac anatomy and function in centenarians and, thus, help us to better understand the process of aging and exceptional longevity. Most centenarians have ECG alterations, and abnormalities in echocardiography are almost universal. One-fifth present atrial fibrillation, and these have echocardiographic evidence of diastolic dysfunction; and left ventricular enlargement. LV dilatation was present in 14% and was independently associated with the ability to walk 6 meters. Aortic regurgitation was found in 49% and was associated with mortality. Our data suggest an age-related effect on the heart that influences functional status and prognosis. This effect should be taken into account in the development of possible strategies to prevent or mitigate it.

2250 | BEDSIDE
Self-detection of atrial fibrillation in aged population - 1-year follow-up of LietoAF study
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Background: Disabling stroke is often the first manifestation of atrial fibrillation (AF) in older subjects. Our objective was to assess motivation and capability of older people to learn pulse palpation and consecutively to register pulse measurements, and to evaluate whether this kind of self-assessment is helpful to detect silent AF.
Methods: A total of 205 persons aged >75 years were randomly selected to participate in the programme where a trained nurse gave a maximum of ten minutes individual education on pulse palpation. The success of training and outcome events were evaluated during follow-up at 1, 4 and 12 months.
Results: A total of 139 subjects (68%) learned the pulse palpation and performed regular palpation during the 1 month follow-up period. Their motivation to regular daily pulse palpation gradually declined from 86% at 4 months to 10% at 12 months. During the 1 year follow-up, new AF was found in 57 patients (4.5% vs. 1.6%; p=0.01), and received lower warfarin prescription (39.1% vs. 41.3%; p=0.01) and anticoagulation therapy. Men had lower CHADS2 score (4.5% vs. 1.6%; p=0.01) and received lower warfarin prescription (39.1% vs.

Figure 1. Infarct size.

Conclusion: The cardioprotective effect of IPC is preserved during MH and adds further protection to the cardioprotective effect of MH during ischemia. The additive cardioprotective effect and differences in metabolism during ischemia may reflect different cardioprotective targets by MH and IPC.
52.2%; p < 0.01). During one-year follow-up, there were more stroke events in super-elderly patients (5.2% vs. 2.1%; p < 0.01), but there was no significant difference in bleeding (5.2% vs. 4.1%; p = 0.31). All-cause death and hospitalization for heart failure were more in super-elderly patients (20.8% vs. 5.9%; p < 0.01, and 7.2% vs. 3.5%; p < 0.01, respectively). Among super-elderly patients, those with atrial fibrillation paradoxically showed a trend toward increased stroke events compared with those without, although not statistically significant (7.5% vs. 3.7%; p = 0.08), whereas no significant difference in bleeding (5.2% vs. 5.2%; p < 1.0). In addition, stroke events were comparable between female and male patients (6.6% vs. 8.5%; p = 0.37), but bleeding was less in female patients (2.8% vs. 9.9%; p < 0.01).

Conclusions: Elderly patients with AF showed higher incidence of stroke, but no significant increase in bleeding, perhaps due to under-use and under-dose of oral anticoagulants in the real-world clinical practice.

2252 | BEDSIDE
Impact of statin therapy on cardiovascular outcomes after coronary revascularization in elderly patients: observations from the CREDO-kyoto registry cohort-2
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Background: Statin therapy has demonstrated the primary and secondary preventive effects in cardiovascular disease in middle-aged population. However, effects of statin therapy on cardiovascular outcomes in elderly population after coronary revascularization, especially in those aged over 80 years, have not been fully elucidated.

Methods: Among 14834 patients undergoing first coronary revascularization in 2005-2007 in the CREDO-Kyoto registry cohort-2, patients were divided into 2 strata based on the age and patients in each stratum were further divided into 2 groups based on the statin therapy at discharge; the ≥ 80 years old stratum: 2017 patients (statin group: N=765, non-statin group: N=1252) and the < 80 years old stratum: 12817 patients (statin group: N=6852, non-statin group: N=6294).

Results: Through 5-year follow-up, cumulative incidences of major adverse cardiovascular events (MACE: composite of cardiovascular death, myocardial infarction and stroke) were significantly lower in the statin group than in the non-statin group in both strata (23.4% vs.32.0%, P=0.0013 in the ≥ 80 years old stratum and 11.5% vs. 16.1%, P < 0.001 in the < 80 years old stratum). After adjusting for confounding factors, statin therapy significantly reduced the risk for MACE not only in those aged ≥ 80 years (adjusted hazard ratio (HR) 0.82, 95% confidence interval (CI) 0.74-0.91, P=0.001) but also in those aged < 80 years (adjusted HR 0.77, 95% CI 0.62-0.93, P=0.009). Statin therapy was also associated with significantly lower risks for all-cause death (adjusted HR 0.76, 95% CI 0.64-0.90, P < 0.001, in the ≥ 80 years old stratum and adjusted HR 0.77, 95% CI 0.69-0.86, P < 0.001, in the < 80 years old stratum) and cardiovascular death (adjusted HR 0.74, 95% CI 0.57-0.94, P < 0.01, in the ≥ 80 years old stratum and adjusted HR 0.76, 95% CI 0.66-0.89, P < 0.001, in the < 80 years old stratum).

Conclusions: Statin therapy significantly reduced the risk for cardiovascular events even in the elderly individuals aged over 80 years. Statin therapy should be considered even in those elders after coronary revascularization.

2253 | BEDSIDE
Age-gender interaction in the prediction of incident cardiovascular disease based on GFR in patients with CKD stages 1-2
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Purpose: Contact force (CF) sensing catheters are becoming the standard for ablation procedures and provide advantages regarding safety and efficacy. This study aimed to evaluate if CF catheters reduce cardiac perforations and other major complications during ablation procedures and offer equal safety compared to the magnetic navigation system (MNS).

Methods: Data from 1.517 ablation procedures from our prospective registry were analyzed. Ablations were performed using either CF guided catheters (CF group, n=248), non-CF catheters (nCF group, n=813), or MNS (n=456). Four subgroups were analyzed: atrial fibrillation (AF, n=557), supraventricular tachycardia (SVT, n=715), ventricular tachycardia (VT, n=190) and pts with congenital heart defects (CHD, n=55). The primary endpoint of this study was incidence of cardiac perforation. Secondary endpoints were major complications (death, tamponade, major bleeding, thromboembolic event, permanent AV block) and minor complications (intraoral hemostasia, temporary AV block) within 30 days of the procedure.

Results: Complications occurred in 11.3% (n=172) of the procedures. In 2.8% (n=43) a major complication occurred, 0.9% (n=13) had a perforation, 8.5% (n=129) had a minor complication and 2 pts died (0.1%). No cardiac perforation occurred in the CF group, which was significantly different from nCF procedures (0.0% vs. 1.6%; relative risk 0.76, 95% CI 0.74-0.79, p < 0.01) and equal to MNS (0.0%). This was also observed in the AF subgroup (0.0% vs. 3.3%; RR 0.07, 95% CI 0.63-0.72, p < 0.001). The occurrence of major complications was lower for CF guided procedures (2.1% vs. 7.8%, p < 0.01). For CF guided AF procedures the average force per RF application was 9.6 ± 4.3 g: the maximum force was 28.4 ± 14.5 g; the force-time integral was 300 ± 158 gs. For the SVT, VT and CHD subgroups perforation rates were not different between CF and nCF procedures (0.0% vs. 0.2%, p=0.883; 0.0% vs. 3.0%, p=0.378; 0.0% vs. 0.0%, p=NA, respectively).

Conclusion: CF-guided catheter ablation is superior to nCF and non-inferior to MNS procedures with regard to procedural safety and avoids cardiac perforation. This difference is due to a reduction of cardiac perforation and major complications in the AF subgroup.
2264 | BEDSIDE
Impact of hospital volume on complication rate of catheter ablation in patients with atrial fibrillation
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Purpose: Although catheter ablation of atrial fibrillation (AF) is commonly performed throughout the world, data regarding complication rates of the procedures are limited to those from high-volume centers. Moreover, previous data lacked information about the impact of hospital volume on complication rates in catheter ablation of AF. We therefore investigated the relationship between hospital volume and complication rate of AF ablation using a national inpatient database.

Methods: Using the Japanese Diagnosis Procedure Combination database between 2010 and 2013, we extracted AF patients who underwent catheter ablation. We performed multilevel logistic regression analyses fitted with generalized estimating equations with hospital as random effect. We compared complication rates between low- (<100 cases/year), medium- (100–199 cases/year) and high-volume (>200 cases/year) hospitals.

Results: Of 32574 AF patients, 460 patients experienced complication. Compared to the lowest-volume group, likelihood of complication for the highest-volume groups was significantly low [Odds ratio, 0.81; 95% confidence interval, 0.39–0.95].

Conclusions: Patients who underwent AF ablation at the very-high-volume hospitals experienced significantly less complication than those at the very-low-volume hospitals. We need to consider regionalization of AF ablation to provide better quality of the procedures.

2265 | BEDSIDE
Novel oral anticoagulants vs continuous warfarin peri-ablation of atrial fibrillation: a meta-analysis of embolic and bleeding complications
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Introduction: Continuous warfarin (CW) has become a preferred peri-ablation strategy for pts with atrial fibrillation (AF). However, novel oral anticoagulants (NOAC) have overtaken W in the non-ablation setting. There are concerns that peri-AF ablation use of NOAC may be associated with worse outcome than CW, but individual studies may be too small given low procedural complication rates. More robust data analyses would be of great value.

Methods: We conducted a meta-analysis of all published papers (n=9) and abstracts (n=10) to date that compared complication rates for peri-AF ablation use of NOAC vs. CW. Bleeding complications included pericardial effusion, groin hematoma, GI bleeding and embolic complications included stroke/TIA or systemic embolism. We used the Mantel-Haenszel fixed effect model for pooling the study results, with a random effects model for heterogeneous samples/results.

Results: The 2578 pts on a NOAC (87.4% dabigatran) were similar to the 3291 pts on CW. NOAC were stopped 2.5–96 hrs pre- and restarted 1–48 hrs post-procedure. Composite bleeding rates were significantly lower in NOAC pts (5.35% vs CW pts (6.87%), (OR 0.74, 95% CI 0.59–0.93; I2 = 26%). Composite embolic rates were similar in both groups (0.50% in NOAC vs 0.43% in CW, OR 1.05, 95% CI 0.53-2.05; I2 = 0%; Figure)

Conclusions: This meta-analysis demonstrates that NOAC are a legitimate alternative for peri-AF ablation anticoagulation. They are associated with a decrease in bleeding and no significant increase in embolic events compared to CW. However, a randomized study to evaluate the two anticoagulation strategies is needed, and to determine optimal time to discontinue and resume NOAC therapy.

2266 | BEDSIDE
Discontinuation period and periprocedural events of novel oral anticoagulants in patients undergoing catheter ablation of atrial fibrillation
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Introduction: The optimal strategy for peri-procedural anticoagulant for radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF) is unknown, especially in patients receiving novel oral anticoagulant (NOAC).

Methods: We performed multilevel logistic regression analyses fitted with generalized estimating equations with hospital as random effect. We compared complication rates between low- (<100 cases/year), medium- (100–199 cases/year) and high-volume (>200 cases/year) hospitals. We need to consider regionalization of AF ablation to provide better quality of the procedures.

Results: Of 32574 AF patients, 460 patients experienced complication. Compared to the lowest-volume group, likelihood of complication for the highest-volume groups was significantly low [Odds ratio, 0.81; 95% confidence interval, 0.39–0.95].

Conclusions: Patients who underwent AF ablation at the very-high-volume hospitals experienced significantly less complication than those at the very-low-volume hospitals. We need to consider regionalization of AF ablation to provide better quality of the procedures.

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Novel oral anticoagulants vs continuous warfarin peri-ablation of atrial fibrillation: a meta-analysis of embolic and bleeding complications
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Introduction: Continuous warfarin (CW) has become a preferred peri-ablation strategy for pts with atrial fibrillation (AF). However, novel oral anticoagulants (NOAC) have overtaken W in the non-ablation setting. There are concerns that peri-AF ablation use of NOAC may be associated with worse outcome than CW, but individual studies may be too small given low procedural complication rates. More robust data analyses would be of great value.

Methods: We conducted a meta-analysis of all published papers (n=9) and abstracts (n=10) to date that compared complication rates for peri-AF ablation use of NOAC vs. CW. Bleeding complications included pericardial effusion, groin hematoma, GI bleeding and embolic complications included stroke/TIA or systemic embolism. We used the Mantel-Haenszel fixed effect model for pooling the study results, with a random effects model for heterogeneous samples/results.

Results: The 2578 pts on a NOAC (87.4% dabigatran) were similar to the 3291 pts on CW. NOAC were stopped 2.5–96 hrs pre- and restarted 1–48 hrs post-procedure. Composite bleeding rates were significantly lower in NOAC pts (5.35% vs CW pts (6.87%), (OR 0.74, 95% CI 0.59–0.93; I2 = 26%). Composite embolic rates were similar in both groups (0.50% in NOAC vs 0.43% in CW, OR 1.05, 95% CI 0.53-2.05; I2 = 0%; Figure)

Conclusions: This meta-analysis demonstrates that NOAC are a legitimate alternative for peri-AF ablation anticoagulation. They are associated with a decrease in bleeding and no significant increase in embolic events compared to CW. However, a randomized study to evaluate the two anticoagulation strategies is needed, and to determine optimal time to discontinue and resume NOAC therapy.

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Discontinuation period and periprocedural events of novel oral anticoagulants in patients undergoing catheter ablation of atrial fibrillation
S. Hiros, K. Miyamoto, I. Nakajima, K. Ishibashi, H. Okamura, T. Noda, T. Alba, S. Kamakura, K. Kusano. National Cerebral and Cardiovascular Center, Division of Cardiology, Saita, Japan
Atrial fibrillation: How to improve the outcomes / Focus on diabetes

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Left atrial size is more important than the type of atrial fibrillation in predicting the long-term success of catheter ablation

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Purpose: The efficacy of atrial fibrillation (AF) catheter ablation in patients with persistent AF and normal or normal-sized left atrium (LA) or with paroxysmal AF and dilated LA is not well established. The purpose of this study was to assess the predictors of outcome after AF ablation, focusing on the interplay between LA size and type of AF.

Methods: We assessed 809 consecutive patients with symptomatic drug-refractory AF undergoing 905 percutaneous pulmonary vein isolation procedures in two different centers. LA volume was assessed by cardiac CT prior to AF ablation. The study endpoint was symptomatic and/or documented AF recurrence.

Results: The majority of patients (73.2%, n = 592) had paroxysmal AF, and the mean indexed LA volume was 55.5 ± 20.2 mm³/m². During a mean follow-up of 2.4 ± 1.7 years, there were 525 recurrences (no blanking period). The relapse rate of patients with paroxysmal AF was higher than the relapse rate of patients with non-paroxysmal AF in the highest tertile of indexed LA volume (p < 0.001, for both).

Conclusion: COLchicine treatment after pulmonary vein isolation for paroxysmal AF is associated with lower AF recurrence rate after a single procedure. This reduction is accompanied by corresponding improvements in physical- and psychological-health-related QoL scores.

Conclusion: When selecting patients for AF ablation, more importance should be given to LA volume than to the type of AF.

Poster Session 3

FOCUS ON DIABETES

P2272 | BESIDE

Impaired fasting glucose is independently associated with left ventricular diastolic dysfunction among middle-aged adults

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Purpose: Left ventricular diastolic dysfunction (LVDD) is the initial echocardiographic derangement in diabetic cardiomyopathy. However, data are limited on the association between impaired fasting glucose (IFG) and LVDD. The aim of the current study was to investigate whether IFG is associated with LVDD among middle-aged adults.

Methods: We investigated 3,201 subjects who were annually screened, had their baseline fasting glucose level documented, and completed Doppler echocardiography. LVDD was diagnosed according to current guidelines based on pulsed-wave Doppler examination of mitral inflow and Doppler tissue imaging of the mitral annulus. Final study population included 2,972 patients and was divided into three groups: euglycemia (NGT; <100 mg/dL or non-IFG = 126 mg/dL); impaired fasting glucose (IFG; 100 mg/dL or non-IFG = 140–199 mg/dL); and normal glucose tolerance (NGT; <126 mg/dL, non-IFG = 126 mg/dL). Categories of BMI, calculated as weight (kg) divided by height (m) squared, were defined as: underweight (<18.5 kg/m²), normal weight (18.5 to <25 kg/m²), and overweight (≥25 kg/m²).

Results: During the 13 years of follow-up, 253 incident AF events occurred (4.2 for men and 1.7 for women per 1,000 persons years). CIFG and DM were not observed increased risk of incident AF (adjusted HRs = 1.08 and 1.32; 95% CI = 0.82–1.42 and 0.78–2.23, respectively). Compared with normal weight, the adjusted HR (95% CIs) of incident AF for overweight was 1.35 (1.01–1.80), and for DM overweight was not linked to an increased risk of incident AF. The interactions between sex and DM and BMI for incident AF were not significant. After omitting the non-fasting subjects (3.4%), all of the results were similar.

Conclusion: With overweight is an important risk factor for incident AF. Appropriate body weight is important for preventing AF in DM populations.

Prevalence of diastolic dysfunction.

Conclusion: IFG is independently associated with LVDD among middle-aged adults. Our findings support the early evaluation of diastolic function in this population.
P2274 | BEDSIDE
Advanced glycation end-products are associated with left ventricular structure and function primarily in individuals with normal glucose metabolism -The Hoorn Study-

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Purpose: Type 2 Diabetes (T2D) is characterized by unfavorable structural and functional cardiac alterations. The accumulation of advanced glycation end-products (AGEs) is believed to play an important role in the pathobiology of this phenotype. Population-based data on the role of AGEs is lacking.

Therefore, the purpose of the study was to investigate the association between the plasma AGEs, NE-carboxyethyl-lysine (CML), pentosidine and NE-carboxymethyl-lysine (CEL), and left ventricular (LV) structure and function, in particular with normal glucose metabolism (NGM), impaired glucose metabolism (IGM) and T2D.

Methods: In this population-based, cross-sectional, study (N=693; 280 NGM, 171 IGM and 242 T2D) participants underwent a standardized echocardiogram. The protein-bound plasma levels of CML, pentosidine and CEL were measured. The analyses were stratified according to plasma glucose status and adjusted for: sex, age, prior cardiovascular disease, hypertension and (or) the use of anti-hypertensive medication (including ace-inhibitors), total cholesterol, smoking, estimated glomerular filtration rate and waist circumference. Linear regression analysis was used to investigate the associations between the individual AGEs and both LV structure and function.

Results: After adjustment, plasma CML was positively associated with both left atrial (LA) volume index and LA volume x LV mass index (both diastolic function parameters) in NGM only (regression coefficient (β) (95%CI): 0.053 (0.011; 0.095) and 0.064 (0.002; 0.126), respectively). Pentosidine was positively associated with both LA volume index and LA volume x LV mass index in NGM (0.056 (0.013; 0.099) and 0.050 (-0.003; 0.164), respectively). Diastolic function was not associated with any of the AGEs in T2D. Systolic LV function (i.e. ejection fraction) was negatively associated with CML in NGM (-1.221 (-2.311; -1.131) and positively associated in T2D (0.937 (0.137; 0.993), p<0.05).

Conclusions: In NGM, both plasma CML and pentosidine were positively associated with diastolic dysfunction and CML was negatively associated with systolic function. In IGM a similar pattern emerged, though less consistent, whereas in T2D diastolic associations with the either non-existent or reversed. The latter suggests that the role of plasma AGEs in the pathobiology of cardiac structure and function changes with deteriorating glucose metabolism.

P2275 | BEDSIDE
Pitavastatin reduced C-reactive protein without increasing the incidence of diabetes in Japanese individuals with impaired glucose tolerance (J-PREDICT study)

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Purpose: Statins may increase the incidence of diabetes mellitus (DM) are more prone to stroke than non-DM patients. Cardiotonic atherosclerosis is a major cause of stroke. Although there are lots of reports that it is implicated in the progression of atherosclerosis seems to be pronounced in patients with DM, similar cardiotonic plaque ultrasound characteristics and distributions have been shown in both patient groups. The aim of this study was to evaluate the impact of DM on morphological and functional cardiac artery structures and plaque composition in patients with DM.

Methods: Consecutive patients (n=333) with significant CAD documented by coronary angiography were evaluated by: 1) Ultra-sound echo-color Doppler (US-ECO) study of both carotid arteries, and 2) microwave radiometry (MR), a new non-invasive method, which allows the in vivo measurement of the internal temperature of tissues reflecting local inflammation. During ultrasound, intima-media thickness of common carotid arteries (cIMT) was measured. Carotid plaques were identified as local intima-media thickening ≥1.2mm and were evaluated for their thickness. AT by MR was defined as the maximum temperature difference of both carotid arteries. Vessel- and patient based analysis were performed to determine the impact of DM on morphological and functional carotid artery characteristics.

Results: One-hundred-twenty seven patients had DM (38.1%). Carotid plaques were identified in 110 patients with DM and in 179 patients without DM (86.6 vs 88.9, p<0.04). Patients with DM had similar cIMT in both vessel- and patient-based analysis (0.97 ± 0.20 versus 1.00 ± 0.12mm, p=0.06; 0.94 ± 0.02 versus 0.94 ± 0.01 mm, p<0.93, respectively). Patients with DM had similar carotid plaque thickness in both vessel- and patient-based analysis (1.97 ± 0.97 versus 2.07 ± 1.01mm, p=0.23; 2.22 ± 0.99 versus 2.47 ± 1.23mm, p=0.06, respectively). Interestingly, patients with DM exhibited higher AT in both vessel- and patient-based analysis (0.81 ± 0.66 versus 0.61 ± 0.64°C, p<0.001; 1.05 ± 0.62 versus 0.84 ± 0.62°C, p<0.001, respectively).

Conclusions: Functional abnormalities may be more profound to structural changes in patients with non-significant carotid artery stenosis and DM. The impact of these functional carotid artery characteristics on patient prognosis still remains to be elucidated.

P2277 | BEDSIDE
Relation between endothelial function and exercise-induced myocardial ischemia in type 2 diabetic patients


Purpose: A significant number of asymptomatic patients with type 2 diabetes mellitus (T2DM) develops significant ST-segment depression (STD) (>1 mm) during exercise stress test (EST), suggesting myocardial ischemia (MI) related to either macrovascular or microvascular coronary artery disease. Aim of this study was to assess whether there is any relation between endothelial dysfunction and EST-induced myocardial ischemia in this kind of patients.

Methods: We studied 100 non insulin-dependent T2DM patients (age 62.7±8.8 years, 70 males; 30%) without any basal or evidence of cardiovascular disease. All patients underwent a symptom/sign limited EST and assessment of the endothelium-dependent function through measurement of flow-mediated dilatation (FMD) following 5-minute forearm ischemia of the right brachial artery. Endothelium-independent function was also assessed through nitrate-mediated dilatation (NMD) of the right brachial artery in response to sublingual administration of 25 μg of nitroglycerin.

Results: STD (horizontal or downsloping STD >1 mm) during EST was induced only in 30% of patients (22%, group 1), whereas 78% (78%, group 2) showed normal ECG during the test. No differences in age, gender, cardiovascular risk factors, drug therapy, blood glucose and glycolated haemoglobin levels were observed between the 2 groups. However, group 1 patients, compared to group 2, showed significa...
P2279 | BEDSIDE
Endothelial glyocalyx is similarly impaired in diabetic patients and first degree relatives and is linked with abnormal aortic elastic properties and myocardial deformation
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The integrity of endothelial glyocalyx plays a vital role in vascular permeability, inflammation and elasticity. The association between damage of endothelial glyocalyx, impaired elastic arterial properties, and LV function in diabetics and first degree relatives has not been explored.

Methods: In 40 unrelated patients (age: 51±12 years) with newly diagnosed type II diabetes, 20 first degree relatives with normal oral glucose tolerance test and 20 controls of similar age and sex and no atherosclerotic risk factors we measured: a) carotid-femoral pulse wave velocity (PWVc m/sec-Complior SP ALAM), central systolic blood pressure (systBP-mmHg), augmentation index (AI%), reflection time (RT-ms) and distal reflection area (DRA) of the aortic pulse wave, an index of coronary perfusion (Arteriograph TensionMed); b) S’, E’ (m/sec) and E/A’ of mitral annulus by Tissue Doppler; c) LV longitudinal strain (GLS, %), systolic (LongSr, 1/sec) and diastolic (LongSrE, 1/sec) strain rate, using speckle tracking echocardiography; d) perfusion boundary region (PBR, μm) of the sublingual microvessels (ranged from 5 to 25 μm) using Sideview, Darkfield imaging (Microscan, Glycocheck). The PBR in microvessels is the cell-layer which results from the phase separation between the flowing red blood cells (RBC) and plasma. The PBR includes the most luminal part of glyocalyx that does allow cell penetration. Increased PBR is considered an accurate index of reduced endothelial glyocalyx thickness because of a deeper RBC penetration in the glyocalyx.

Results: Compared to controls, diabetics and relatives had higher PBR (2.1±0.25 vs. 2.05±0.25 vs. 1.89±0.11 A1 (27±16 vs. 24±15 vs. 17±14 and DRA (44±12 vs. 49±13 vs. 68±27), p<0.05). Diabetics and relatives had similar PBR, AI and DRA (p=ns). Compared to controls, diabetics had also higher PWV (10.9±2 vs. 8.9±2, p<0.05), central systolic blood pressure (systBP) (~4±~3 mmHg, p<0.05). Reduced endothelial glyocalyx thickness as assessed by increased PBR was related with increased PWV (r=0.35, p<0.05), reduced RT (~r=0.42 and DRA (~r=0.36 in diabetics (p<0.05). These associations were more pronounced in relatives compared to controls.

Conclusion: Endothelial glyocalyx is impaired in newly diagnosed diabetics and first degree relatives and is related with abnormal aortic elastic properties leading to impaired LV longitudinal deformation in diabetics.

P2277 | BEDSIDE
Asymptomatic low fasting blood glucose is associated with enhanced thrombin generation and unfavorable fibrin clot properties in patients with type 2 diabetes and high cardiovascular risk
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Objective: To evaluate the effect of low blood glucose on fibrin clot formation, properties and degradation in type 2 diabetes mellitus (T2DM).

Methods: In 165 patients with T2DM and high cardiovascular risk, we measured ex vivo plasma clot lysis time [t50%], together with thrombin generation and platelet activation markers in relation to fasting blood glucose.

Results: Patients with asymptomatic low fasting glucose (~4.5 mmol/l) (~r=38 had lower Ks (~1%-1%, p<0.001, prolonged IS0 (~10%, p<0.001, higher peak thrombin generation (~21.3%, p<0.002) and a trend towards higher plasma CD40 ligand (~16.2%, p=0.09) as compared to patients with glucose >4.5 mmol/l (~r=127). Kinetics of fibrin formation was unaffected by low glucose. There was a U-shape type of relationship between glycemia and peak thrombin generation, Ks and IS0. In patients with HbA1c ~6.0% (~n=26) there were the most potent correlations between fasting glucose and both Ks (~r=0.53, p<0.006) and IS0 (~r=0.46, p<0.02). Fasting glucose concentration influenced Ks (F=7.82, p<0.0006), IS0 (~F=9.24, p=0.0002) and PF4 even after adjustment for age, fibrinogen, HbA1c and T2DM duration.

Conclusions: In T2DM patients fasting glycaemia <4.5 mmol/l is associated with enhanced thrombin formation and formation of denser fibrin clots displaying lower lysisability, especially when strict glycemia control was achieved (HbA1c~6.0%). Our findings may partly explain increased cardiovascular risk in T2DM patients on intensive glucose lowering treatment.

P2280 | BEDSIDE
High adiponectin and reduced risk of T2DM in patients with STEMI
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Background: Adiponectin is an insulin-sensitizing hormone with anti-inflammatory effects produced in adipose tissue. Plasma adiponectin is decreased to several metabolic disorders including type 2 diabetes mellitus (T2DM), and in healthy humans, high adiponectin associates with reduced risk of T2DM. However, little is known of the relationship between adiponectin and T2DM in patients with myocardial infarction, where adiponectin is elevated and associated with a poor prognosis. Accordingly we investigated adiponectin and risk of T2DM in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: We prospectively included 735 patients with STEMI treated with primary PCI, from September 2006 to December 2008 at a tertiary cardiac centre. Blood samples were drawn immediately before PCI, and total plasma adiponectin measured in all samples. Patients were followed for 5 years. Risk of T2DM was analysed using a competing risk analysis.

Results: Higher adiponectin associated with decreased risk of T2DM (p<0.001). Even after adjustment for confounding risk factors (age, gender, hypertension, hypercholesterolemia, previous MI, BMI, blood-glucose, eGFR, CRP, peak-TnI and proANP) higher adiponectin remained an independent predictor of reduced risk of T2DM: hazard ratio for 1 SD increase in adiponectin (log2-transformed): 0.42 (95% CI 1.24-1.74; p<0.003). Importantly, high adiponectin added to the predictive value of blood-glucose, with the combination of high blood glucose and low adiponectin vastly increasing the risk of T2DM, HR 11.7 (4.5-31.0, p<0.001).

Conclusions: Higher plasma adiponectin is independently associated with decreased risk of T2DM in patients with MI. Importantly, adiponectin added significantly to the predictive value of blood-glucose.
Results: In our population of diabetic patients with a high prevalence of statin therapy (89%), inadequate control of the levels of LDL (LDL -70 mg/dL) was not associated with a greater CA progression. However, diabetic patients with inadequate control of both HDL and TG (HDL <40 mg/dL and TG >150 mg/dL) showed significantly most CA progression as measured by the ΔTAVG (7.7±2.1 mm² vs -3.7±19.3 mm², p=0.006) and by the ΔPAV (1.2±4.9% vs -0.5±5.3%, p=0.034).

Conclusions: Diabetic dyslipidemia (low HDL and high triglyceride levels) is associated with increased CA progression. These findings suggest the need for intensive lipid control in diabetic patients with coronary artery disease, with especial emphasis to obtain adequate control of HDL and TG levels.

P2282 | BEDSIDE
Right ventricular and right atrial deformation in normotensive patients with prediabetes and type 2 diabetes mellitus: a two- and three-dimensional strain analysis

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Objective: To evaluate right ventricular (RV) and right atrial (RA) deformation obtained by 2D (3DE) and three-dimensional echocardiography (3DE) in patients with prediabetes and type 2 diabetes mellitus.

Methods: This cross-sectional study included 51 untreated normotensive subjects with prediabetes, 60 recently diagnosed normotensive untreated diabetic patients, and 55 age-matched and sex-matched controls of similar body mass index. All the subjects underwent laboratory analyses and comprehensive 2DE and 3DE examination.

Results: 3DE RV end-diastolic volume index progressively reduced from the controls throughout the prediabetics to the diabetics (70±10 vs. 64.8 ± 8.7 vs. 57.8 ± 8.6 ml/m², p<0.01). Similarly, 3DE RV end-systolic volume index was higher in the controls comparing with the prediabetics and the diabetics (26.1±4 vs. 24.4 ± 4 vs. 22.4±4 ml/m², p<0.01). There was no difference in 3DE RV ejection fraction among the three groups (63±4 vs. 62.6±5 vs. 61.6±5, p>0.05). 3DE RV wall thickness was increased in patients with prediabetes and diabetes comparing with the controls (27.5±5 vs. 26.3±4 vs. 24.4±4% for RV strain, p<0.01). The same results were obtained for RA global strain (45.3±8 vs. 40.1±7 vs. 37.7±7%, p<0.01), as well as for RV and RA systolic and early diastolic strain rates, whereas RV and RA lateral strain were lower in AGI individuals. The fasting blood glucose level correlated with 3DE RV end-diastolic strain rate (r=-0.26, p=0.04).

Conclusions: Right ventricular and right atrial deformation evaluated by 3DE demonstrate the adverse effects of prediabetes and type 2 diabetes mellitus on myocardial mechanics and function.

P2283 | BEDSIDE
Identifying prediabetes in essential hypertensive patients with the findrisc questionnaire

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Objective: The Finnish Diabetes Risk Score questionnaire (FINDRISC) is a practical validated tool to estimate the risk for future type 2 diabetes mellitus (T2DM). This study sought to evaluate the potential associations of the FINDRISC with the metabolic profile of newly-diagnosed essential hypertensives (EH).

Design and methods: 757 consecutive non-diabetic patients (52±13 years, 53% males, body mass index 29±4 kg/m²) were studied. Fasting plasma glucose (FPG), 2-hour post-load glucose (2hPG) and HbA1c were measured. Patients with all three measures in the normal range were considered as euglycemic, while those with more than one measure in the prediabetic range were considered as having advanced glycemic impairment (AGI). Age, BMI, waist circumference, history of antihypertensive drug treatment, and blood glucose, physical activity and daily consumption of fruits and vegetables were determined for the calculation of FINDRISC. The score ranges from 0 to 26 points with higher score repre-resenting higher 10-year risk.

Results: The glycemic profile of the participants was as follows: euglycemic 56.34%, impaired fasting glucose (IFG) 22.8%, impaired glucose tolerance (IGT) 0.26%, impaired HbA1c 10.6%, while 10% of the patients presented AGI. The prevalence of pre-diabetes and metabolic syndrome (MS; IDF criteria) was 48% and 53%, respectively. Regarding FINDRISC, 13.4% of patients had score <-7, 37.1% 7-11, 21.6% 12-14, 24.1% 15-20 and 3.8% >20. Euglycemic patients had score 10±4 while pre-diabetics 14±4 (p<0.05). MS patients had FINDRISC 14±4 while non-MS patients 9±4 (p<0.05). The score was 14±2 in AGI, 13±4 in IFG (p<0.05 vs normal), and 20±4 in IGT. Almost 90% of patients with score ≥12 had at least one glycemic measure abnormal, while 67% of those with score ≥12 had all measures normal. FINDRISK was correlated to FPG (r=0.32, p<0.001), 2hPG (r=-0.23, p=0.027) and HbA1c (r=0.29, p<0.001). The area under ROC curve for FINDRISC to detect dysglycemia was 0.67 (95%CI 0.63-0.71), with the optimal cut-off level being 11 points (sensitivity 72%, specificity 61%).

Conclusions: Almost half of middle-aged, newly-diagnosed hypertensives are prediabetic. The FINDRISC is proved as a useful, cost-effective tool for identifying these individuals.

P2285 | BEDSIDE
Association of genetic variants of the alpha-kinase 1 gene (ALKP1) with type 2 diabetes mellitus in community-dwelling Japanese individuals

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Purpose: We previously showed that genetic variants of the alpha-kinase 1 gene (ALKP1) were significantly associated with chronic kidney disease in Japanese individuals with diabetes mellitus by a genome-wide association study. Although genetic variants in ALKP1 were related to chronic kidney disease for individu-als with diabetes mellitus, the association of ALKP1 with type 2 diabetes mellitus has not been elucidated. The purpose of the present study was to ex-amine a possible association of rs2074388 (G→A, Gly565Asp) and rs2074379 (G→A, Met732Ile) of ALKP1 with type 2 diabetes mellitus in community-dwelling Japanese individuals.

Methods: Study subjects comprised 5959 community-dwelling individuals (495 subjects with type 2 diabetes mellitus, 5464 controls) who were recruited to a population-based cohort study in Inabe City, Japan. Subjects with type 2 dia-betes mellitus had a fasting plasma glucose level of ≥7.0 mmol/L, or a blood glycosylated hemoglobin (hemoglobin A1c) content of ≥6.5% or were taking antidiabetes medication. The control individuals had a fasting plasma glucose level of <6.0 mmol/L and a blood hemoglobin A1c content of <5.6%, and they had no history of diabetes mellitus or of taking antidiabetes medication. Genotypes of polymorphisms were determined by the multiplex bead-based Luminox assay, which combines the polymerase chain reaction and sequence-specific oligonucleotide probes with suspension array technology.

Results: Comparisons of allele frequencies or genotype distributions by the chi- square test revealed that the rs2074388 (allele, P=0.0095; genotype, P=0.0244) and rs2074379 (allele, P=0.011; genotype, P=0.0304) of ALKP1 were significantly (P<0.05) associated with type 2 diabetes mellitus. Multivariable logistic regression analysis with adjustment for age, sex, body mass index, and smoking status revealed that the rs2074388 (G→A, Gly565Asp) and rs2074379 (G→A, Met732Ile) of ALKP1 may be a susceptibility locus for type 2 diabetes mellitus in Japanese individuals.

Conclusions: ALKP1 may be a susceptibility locus for type 2 diabetes mellitus in Japanese individuals.

P2286 | BEDSIDE
Glycemic variability assessed by continuous glucose monitoring and its correlation with renal and myocardial damage after coronary stenting

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Purpose: Previous studies have demonstrated a significant impact of pre-procedural blood glycemic levels (pre-BGLs) on post-procedural myocardial and renal damage in patients undergoing percutaneous coronary intervention (PCI). Recently, the analysis of glucose fluctuations within a predefined interval, defined as glycemic variability (GV), has been shown to estimate patients’ metabolic status better than single spot glycemic determinations. However, its influence on PCI outcomes has not been characterized yet. The aim of this study is to evaluate the correlation between peri-procedural GV, assessed by continuous glucose monitoring (CGM), and myocardial and renal damage, the latter also assessed by the mitochondrial Delaninase-Associated Lipocid (NAL) after coronary stenting.

Methods: GV in the peri-procedural period was continuously monitored by a small subcutaneous device, in 28 patients with diabetes mellitus type 2 undergoing PCI, and measured by multiple indexes: Standard Deviation (SD), Coef-ficients of Variability (CV) in 3DE RV end-systolic volume index (MAGE), Mean Amplitude Glycemic Excursions (MAGE, MAGE up, considering nadir-to-peak fluctuations and MAGE-down, peak-to-nadir excur-sions) and Continuous Overall Net Glycemic Activity (CONGA, measuring intra-day glycemic swings occurring over predetermined intervals: 1 hour, 2 hours, 4
hours). Serum creatinine, NGAL and Troponin I levels were measured before and after PCI.

Results: A significant correlation was observed between NGAL variation and CV (r = 0.394, p = 0.045), SD (r = 0.408, p = 0.043), MAGE (r = 0.407, p = 0.043), MAGE-up (r = 0.467, p = 0.019) and CONGA-4 (r = 0.461, p = 0.021). Moreover, at the multivariate analysis, CONGA-4 remained an independent predictor of NGAL increase (p = 0.042). A similar association was found between GV indexes and serum creatinine variation. Post-procedural increase of Troponin I significantly correlated with CONGA-2 (r = 0.390, p = 0.040). Patients with peri-procedural myocardial infarction showed higher mean values of CONGA-1, CONGA-2 and MAGE-down compared with patients without this complication, with CONGA-1 being an independent risk factor for its occurrence (p = 0.041).

Conclusions: Our results show a significant correlation of GV with renal and myocardial infarction effects on QT dispersion and double products. Autonomic glycemic excursions during the peri-procedural period may provide important diagnostic information and guide individualized therapeutic protocols for euglycemia.

P2287 | BEDSIDE
Alcohol drinking and 10-year incidence of diabetes mellitus: the ATTICA study
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Aim: The aim of this work was to evaluate the nature of a potential dose-response relationship, between alcohol drinking and 10 year incidence of diabetes.

Methods: During 2001-2, 1514 men and 1528 women (â¥18 years) without any clinical evidence of cardiovascular disease (CVD) at the baseline examination, live in Athens, Greece, were examined in the ATTICA study. In 2381, 12, the 10-year follow-up was performed. Several demographic, lifestyle, clinical and biochemical characteristics of the participants, as well as dietary habits, including alcohol consumption (translated to ethanol intake in g/day and type of alcohol drink), were evaluated, in relation to the development of diabetes as defined according to WHO-ICD-10 criteria (fasting blood glucose > 125 mg/dL or the use of antidiabetic medication). Participants were classified based on their daily ethanol intake in two categories: abstention or high consumption. The effect of the type of drink consumed was evaluated using the ratio wine-to-other spirits. In the present work, 1679 participants (47±1.4 yr, 49.9% men) who had no history of diabetes at baseline examination were studied.

Results: The 10-year incidence of diabetes was 11.6% per 100 men and 11.2 per 100 women. 55% of the participants reported at least low alcohol consumption on a weekly basis. Data analysis revealed that abstention or high consumption of alcohol (defined as <10 g for women and <20 g for men) was associated with 2.01-times (95% CI 1.14, 3.53) higher risk of developing type 2 diabetes, as compared to moderate consumption, after taking into consideration age, sex, abnormal waist circumference, physical activity, education, overall diet quality, family history of diabetes and the common cardiovascular risk factors; thus, a U-shaped relationship was evident. When type of alcohol consumed was taken into account, through the ratio wine-to-other spirits, an inverse relationship was observed, i.e. the higher the ratio, the lower the risk of Relative Risk = 0.38, 95% CI 0.55, 1.00, adjusting for the aforementioned factors.

Conclusions: Our results suggest a U-shaped relationship of ethanol consumption and the development of diabetes, within a 10-year period. Furthermore, wine drinking against other spirits ratio exerted a significant protection, underlying the pleiotropic benefits from wine of cardiometabolic risk.

P2288 | BEDSIDE
Impact of short-term exercise training on QT dispersion and double product in diabetic patients after myocardial infarction

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Purpose: The aim of this study was to establish the influence of short-term exercise training on QT dispersion and double product (DP), in diabetic patients after myocardial infarction.

Methods: The study involved 353 patients after myocardial infarction, in the sinus rhythm without AV blocks or branch blocks. Average age of patients was 56.8 years (SD ± 12.3 years). Group was divided into training group (NTG: 42 patients) and non-training group (NTG: 42 patients). Patients were of similar age, site of infarction and baseline stress test duration. Diabetes was present in 102 (32.8%) patients in the TG and in 14 (33.3%) patients in the NTG. In all subjects standard ECG and exercise test on treadmill were performed and after that TG patients were included in rehabilitation treatment for three weeks. TG patients were instructed to follow a training program using the bicycle ergometer (10 min, 2 times a day) and walking. The patients continued to take the same medica-

Results: Before starting with the program of physical training, TG patients with diabetes had significantly higher values of QTdc (80.5±26.2 vs 68.7±23.1 ms; p = 0.001), while the values of DP did not significantly vary (12183.4 ± 1973.4 vs 11882.5 ± 1856.2 beat/min x mmHg; p = 0.35) in comparison to those without diabetes. After three weeks in TG, significant reduction of QTdc was found (30.8±12.6 to 72.7±23.6 ms; p = 0.025 in patients with diabetes and from 68.7±23.1 to 57.4±21.2 ms; p = 0.001 in patients without diabetes). After three weeks in TG, significant reduction of DP was found (from 12183.4 ± 1973.4 to 11578.1 ± 1966.2 beat/min x mmHg; p = 0.02 in patients with diabetes and from 11882.5 ± 1856.2 to 11196.6 ± 1510.3 beat/min x mmHg; p = 0.001 in patients without dia-

Conclusions: The study showed that patients with diabetes have a higher value of QTdc, probably due to diffuse interstitial fibrosis. Short-term exercise training has led to significant improvements in QT dispersion and double product, probably by reducing the myocardial oxygen uptake at rest and probably decreased the possibility of arhythmia events.

P2290 | BEDSIDE
Association of a genetic variant of the zinc finger protein 259 gene with type 2 diabetes mellitus in Japanese individuals
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Purpose: Genetic variants that contribute to susceptibility to type 2 diabetes mellitus in Japanese individuals remain to be identified definitively. Various loci and genes that confer susceptibility to coronary heart disease (CHD) have been identified by two large GWASs in Caucasian populations (GWASs). Given that type 2 diabetes mellitus is an important risk factor for CHD, we hypothesized that some polymorphisms might contribute to the genetic susceptibility to CHD through affecting the susceptibility to type 2 diabetes mellitus. The purpose of the present study was to examine a possible association of type 2 diabetes mellitus in Japanese individuals with 15 polymorphisms identified as susceptibility loci for CHD in the previous GWASs.

Methods: Study subjects comprised 3757 individuals (1444 subjects with type 2 diabetes mellitus, 2313 controls) who visited the participating hospitals between 2002 and 2012. Subjects with type 2 diabetes mellitus had a fasting plasma glucose level of > 7.0 mmol/L or were taking antidiabetic medication. The control individuals had a fasting plasma glucose level of < 6.05 mmol/L and had no history of diabetes mellitus or of taking antidiabetic medication. Genotypes of polymorphisms were determined by the multiplex bead-based Luminex assay, which combines the polymerase chain reaction and sequence-specific oligonucleotide probes with suspension array technology. To compensate for multiple comparisons, we adopted the criterion of a false discovery rate (FDR) of < 0.05 for statistical significances of the association.

Results: Comparisons of allele frequencies by the chi-square test revealed that the rs964184 (G â¥C polymorphism) of the zinc finger protein 259 gene (ZNF259) was significantly (P = 0.0017, FDR = 0.025) associated with type 2 diabetes mellitus. Multivariable logistic regression analysis with adjustment for age, sex, and body mass index revealed that rs964184 of ZNF259 was signifi-

Conclusions: ZNF259 may be a susceptibility locus for type 2 diabetes mellitus in Japanese individuals.

P2299 | BEDSIDE
Hemoglobin A1c is associated with coronary artery calcium in non-diabetic Korean adults
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Introduction: Although many studies have reported that hyperglycemia could contribute to test on treatment and progression of atherosclerosis, limited data have addressed the relationship of hyperglycemia with coronary artery calcification, especially in non-diabetic Asian population.

Objectives: The present study was performed to evaluate the association between hemoglobin A1c (HbA1c) and coronary artery calcium, and hyperglycemia, and coronary artery calcification in non-diabetic Korean adults.

Methods: Coronary artery calcium score (CACS) and HbA1c level were investi-

In a total of 12,853 individuals (10,521 men, mean age, 42±6 years)
who participated in our Health Study between 2010 and 2011. Individuals were divided into 4 groups according to HbA1c quartiles (≤5.4, 5.41-5.60, 5.61-5.80, and >5.80%).

**Results:** The overall prevalence of presence of CAC among total individuals was 9.5%; according to HbA1c quartiles, the prevalence of CAC(+) group was 6.0%, 7.7%, 11.2%, and 15.2% in the lowest, 2nd, 3rd, and highest HbA1c quartiles, respectively. The CAC(+) group had unfavorable cardiometabolic and lipid profiles. In a multivariate regression analysis after adjusting for variables with a univariate relationship (p<0.20), the 3rd and highest quartile group of HbA1c had higher odds ratios (ORs) for the presence of CAC compared with that of the lowest quartile group (OR [95% confidence interval] (CI), 1.131 (0.910, 1.361), 1.413(1.157, 1.726), and 1.670[1.344, 2.076] in the 2nd, 3rd, and highest HbA1c quartiles), and increasing quartiles of HbA1c was also associated with the presence of CAC (p<0.005). In a trend-absolute sliding HbA1c level had a significant relationship with the presence of CAC and increasing CACS, respectively (OR [95% CI] 1.366[1.131, 1.649], p<0.001: standardized (β=0.045, p<0.001, respectively). According to NFG and IFG groups, HbA1c level was associated with CACS in the NFG group (standardized (β=0.045, p<0.001), but the association had a trend toward increasing CACS (standardized (β=0.035, p=0.068) in the IFG group.

**Conclusion:** This study showed an independent relationship between serum hemoglobin A1c level and coronary artery calcification in non-diabetic Korean adults. This could suggest that individuals with increased HbA1c level should be pay particular attention for more accurate cardiovascular risk stratification, even though HbA1c level would not be over diabetic range.

**P2291 | BEDSIDE**

**Predictive value of dysglycemia biomarkers in the prognosis of patients with acute myocardial infarction with and without ST segment elevation**


**Methods:** We enrolled and followed up (median time 9 years) 119 patients (median age 65 years, females 70%) with T2DM and not known CV disease. Arterial stiffness was assessed by measuring carotid-femoral pulse wave velocity (PWV) using arterial tonometry. Endothelial function was assessed by endothelium-dependent vasodilation of brachial artery using ultrasonography. YKL-40, C-reactive protein and NGAL were used as indices of inflammation while retinol binding protein 4 (RBP4) and fatty acid binding protein 4 were used as indices of insulin resistance. The prognostic role of the vascular and biochemical indices for total mortality and CV events during follow-up was assessed using Cox regression analysis.

**Results:** There were 11 deaths (from all causes) and 21 CV events recorded in the follow-up. PWV was positively associated with YKL40 and NGAL (p<0.05 for both). Increased PWV (HR 3.5, p=0.031), YKL40 (HR 2.9, p=0.021) and NGAL (HR 2.5, p=0.05) were associated with the occurrence of CV events in univariate analysis, but only increased PWV (i.e. >10 m/sec) (HR 3.2, p=0.049) remained an independent predictor of CV events after adjustments for classical risk factors. Higher glucose levels and lower body mass index (BMI) were also independently associated with CV events (p<0.05 for both). Total mortality was significantly associated with increased RBP4 in univariate and multivariate analysis (HR 2.3, P=0.015 for a 40% increase in RBP4).

**Conclusions:** In T2DM patients, increased arterial stiffness was associated with arterial inflammation (YKL40 and NGAL). Increased arterial stiffness and hyperglycemia were independent predictors of CV events while BMI showed a paradoxical inverse relation with these events. Insulin resistance as assessed by increased RBP4 was the most important predictor of total mortality in our population.

**P2293 | BEDSIDE**

**Increased arterial stiffness and retinol binding protein 4 are associated with adverse prognosis in type 2 diabetes patients**


**Methods:** In 60 consecutive subjects without known diabetes a standard 75-gr oral glucose tolerance test (OGTT), was performed and plasma glucose and serum insulin levels were measured at 0, 30, 60, 90 and 120min after glucose loading. At the same time intervals, we measured the carotid-femoral pulse wave velocity (PWV) using the Complor apparatus and aortic PWV (PWVs), central blood pressure (cSBP), augmentation index (AI) using an oscilometric method (Arteriograph). We measured insulin resistance a) after fasting, using homeostatic model assessment (HOMA) and hepatic insulin sensitivity (HIS) b) during OGTT using Matsuda index and insulin sensitivity index (ISI).

**Results:** Patients with abnormal OGTT (n=24) had higher baseline PWV (10.3±2 vs. 9.1±1.8 m/sec, p<0.05), PWVs (9.4±1.9 vs. 6.9±1.8 m/sec, p<0.05), AI (24.9±17 vs. 17±11%, p<0.05), insulin (14±6 vs. 11±4 µU/ml, p<0.05), glucose levels (114±26 vs. 93±7 mg/dl, p<0.05), HOMA, (3.7±1.3 vs. 2.7±1.7, p<0.05) and lower HIS (0.34±0.24 vs. 0.46±0.18, p<0.05), ISI (55.8±22 vs. 90±17, p<0.05), Matsuda index (3.2±1.6 vs. 4.5±1.2, p<0.05) and similar age, sex and BMI than those with normal OGTT (p<0.05).

Of all indices, decreasing ISI was best related to increasing PWV, PWVs cSBP and AI measured at baseline (r=0.37, r=-0.63, r=0.30, r=0.45, p<0.05), at 30 min (r=0.39, r=-0.64, r=-0.31, r=-0.46, p<0.05), 60 min (r=-0.44, r=-0.65, r=-0.34, r=-0.47, p<0.05), 90 min (r=-0.52, r=-0.70, r=-0.33, r=-0.48, p<0.05) and 120 min (r=-0.54, r=-0.69, r=-0.30, r=-0.45, p<0.05) during OGTT. Similar associations were observed between Matsuda index and vascular markers (p<0.05). Although, resistance with indexes of subclinical atherosclerosis was also increased, this association was not statistically significant.
Conclusion: HbA1c is significantly associated with CAD and may predict the atherosclerosis (Gensini Undiagnosed glucose metabolism disturbances are common in patients with diabetes. In non-diabetic patients, very few reports have examined the relationship between HbA1c and extent of coronary artery disease.

Objectives: The aim of this study was to examine the relationship between HbA1c level and extent of coronary artery disease (CAD) in non-diabetic patients scheduled for elective coronary angiography.

Methods: We studied 408 consecutive non-diabetic patients (mean age 54.4 ± 9.5 years) with or without previous history of myocardial infarction, who were scheduled for elective coronary angiography due to clinical reasons. All patients had no previous coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting). Extent and severity of CAD was assessed by Gensini score. Gensini score > 30 was considered severe coronary atherosclerosis. Echo-cardiography was done to assess left ventricular ejection fraction (LVEF) and regional wall motion score index (RWMSI) in all patients. Patients were divided into a high risk group (HbA1c 5.7 - 6.4%, n=292) and a low risk group (HbA1c 5.7% - 6.0%, n=116).

Results: Patients in both groups had comparable prevalence of hypertension, smoking and family history of CAD. No significant difference was noted as regards clinical presentation and treatment. Mean ± S.D. LVEF was higher in the high risk group (54.9 ± 9.7 vs. 57.2 ± 9.7, P<0.005). HbA1c showed positive correlation with Gensini score (r=0.243, P<0.000). Patients with Gensini score > 30 had higher values of HbA1c (6.0 ± 0.48 vs. 5.75 ± 0.54, P<0.000). HbA1c value of 5.85 showed a sensitivity of 70% and a specificity of 50% for prediction of severe coronary artery disease (CAD). (95% CI: 0.690–0.990, P<0.000).

Conclusion: HbA1c is significantly associated with CAD and may predict the extent of atherosclerosis in non-diabetic patients.

P2294 | BEDSIDE
HbA1c help prediction of severity of coronary artery disease in non-diabetic patients
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Background: Among the known risk factors for cardiovascular disease, type 2 diabetes mellitus (T2DM) ranks as one of the most potent. It has been recognized that metabolic syndrome (MetS) is associated with increased HbA1c levels in patients with diabetes are risk factors for cardiovascular events and subclinical atherosclerosis. Lowering HbA1c was shown to be associated with reduction of microvascular, neuropathic and possibly macrovascular complications in patients with diabetes mellitus. However, in non-diabetic patients, very few reports have examined the relationship between HbA1c and extent of coronary artery disease.

Objectives: The aim of this study was to examine the relationship between HbA1c level and extent of coronary artery disease (CAD) in non-diabetic patients scheduled for elective coronary angiography.

Methods: We studied 408 consecutive non-diabetic patients (mean age 54.4 ± 9.5 years) with or without previous history of myocardial infarction, who were scheduled for elective coronary angiography due to clinical reasons. All patients had no previous coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting). Extent and severity of CAD was assessed by Gensini score. Gensini score > 30 was considered severe coronary atherosclerosis. Echo-cardiography was done to assess left ventricular ejection fraction (LVEF) and regional wall motion score index (RWMSI) in all patients. Patients were divided into a high risk group (HbA1c 5.7 - 6.4%, n=292) and a low risk group (HbA1c 5.7% - 6.0%, n=116).

Results: Patients in both groups had comparable prevalence of hypertension, smoking and family history of CAD. No significant difference was noted as regards clinical presentation and treatment. Mean ± S.D. LVEF was higher in the high risk group (54.9 ± 9.7 vs. 57.2 ± 9.7, P<0.005). HbA1c showed positive correlation with Gensini score (r=0.243, P<0.000). Patients with Gensini score > 30 had higher values of HbA1c (6.0 ± 0.48 vs. 5.75 ± 0.54, P<0.000). HbA1c value of 5.85 showed a sensitivity of 70% and a specificity of 50% for prediction of severe coronary artery disease (CAD). (95% CI: 0.690–0.990, P<0.000).

Conclusion: HbA1c is significantly associated with CAD and may predict the extent of atherosclerosis in non-diabetic patients.
its components on central aortic pressure (CAP), an excellent surrogate marker of cardiovascular disease, in the general population.

**Method:** CAP was measured in 795 subjects (male=4590, age=56.8±12.0 years) who visited our hospital for a yearly physical checkup from January to December 2012 and a cross-sectional analysis was performed. Brachial blood pressure (BP) (sphygmomanometer), radial artery pressure (sphygmomanometer) and carotid intima-media thickness (IMT) were recorded using an automated device, and CAP was estimated using systolic pressure corresponding to the second systolic peak of radial pressure waves (HREM-9000AI). The MetS was defined according to the Japanese criteria (the presence of two or more of the following items in subjects with obesity, (1) elevated triglycerides and/or decreased high-density lipoprotein cholesterol [dyslipidemia], (2) elevated BP, and (3) impaired glucose tolerance [IGT]).

**Results:** Physical checkup revealed that 1148 subjects had MetS (defined as a mixture of vascular disease risk factors). CAP was higher in subjects with than without MetS (142.9±19.1 vs. 127.8±19.6mmHg). The prevalence of MetS independently predicted an increase in CAP (P<0.0001). Among metabolic factors, obesity and elevated BP were correlated with CAP in multivariate regression analysis. Furthermore, CAP levels were increased with increasing the number of the component of MetS in each individual (without metabolic component, 114.8±12.1; 1 component, 132.1±19.5; 2 components, 138.4±19.0; components ≥3, 142.8±19.1mmHg). In analysis with normotensive subgroups, brachial BP and CAP were higher in subjects with than without metabolic components, but they were not affected by the number of metabolic components. In contrast, in subjects with elevated BP, brachial BP, but not CAP, values were increased with increasing the number of metabolic components (1 component, 136.6±15.6; 2 components, 137.4±15.3; components ≥3, 139.0±16.7mmHg). Similar results were obtained with analysis of subjects using antihypertensive medication (not recorded).

**Conclusions:** The presence of MetS increases CAP. Among metabolic components, obesity and elevated BP were the independent predictors of CAP. Furthermore, the impact of obesity, dyslipidemia or IGT on CAP was affected by brachial systolic pressure. It can be proposed that an increase in body weight and normal brachial BP may contribute to the reduction of cardiovascular risk only at least partially though a reduction in CAP.

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**P2302 | BESIDE**

**Preclinical atherosclerosis and metabolic syndrome increase cardio- and cerebrovascular events rate: a 20-year follow up**

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**Background:** Intima-media thickness (IMT) is a validated marker of preclinical atherosclerosis and a predictor of cardiovascular events.

**Patients:** We studied a population of 529 asymptomatic patients (age 62.2±12.8 years), divided into two groups of subjects with and without Metabolic Syndrome (MetS).

**Methods:** All patients, at baseline, have had a carotid ultrasound evaluation and classified in 2 subgroups: the first one without atherosclerotic lesions and the second one with preclinical atherosclerosis (increased IMT or asymptomatic carotid plaque). Cardiovascular endpoints were investigated in a 20-years follow-up.

**Results:** There were 242 cardiovascular events: 144 among patients with MetS and 98 among healthy controls (57.4% vs. 35.2%; P<0.0001). 63 events occurred in patients with normal carotid arteries, while 179 events occurred in patients with preclinical atherosclerosis (31.8% vs. 54.1%; P<0.0001). Of the 144 total events occurred in patients with MetS, 36 happened in the subgroup with normal carotid arteries and 108 in the subgroup with preclinical atherosclerosis (45% vs. 63.1%; P<0.009). 98 events occurred in patients without MetS, of which 27 in the subgroup with normal carotid arteries and 71 in the subgroup with preclinical atherosclerosis (22.8% vs. 44.37%; P<0.0003). In addition, considering the 63 total events occurred in patients without atherosclerotic lesions, 36 events were recorded in the subgroup with MetS and 27 events in the subgroup without MetS (45% vs. 22.8%; P<0.0015). Finally, in 179 total events recorded in patients with preclinical carotid atherosclerosis, 108 happened in the subgroup with MetS and 71 happened in the subgroup without MetS (63.1% vs. 44.37%; P<0.0099). The Kaplan-Meier function showed an improved survival in patients with preclinical atherosclerotic lesions compared with patients with carotid ultrasound alterations (P<0.01, HR: 0.7366, CI: 0.5479 to 0.9904).

**Conclusions:** Preclinical atherosclerosis lead to an increased risk of cardiovascular events, especially if it is associated with MetS.

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**P2303 | BESIDE**

**Metabolic syndrome (MetS) predicts cardio- and cerebrovascular events in a twenty years follow-up. A prospective study**

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**Background and purpose:** Metabolic Syndrome (MetS) is a cluster of cardiovascular risk factors, considered as emerging and promoting atherosclerosis. This study aimed at the evaluation of the influence of MetS on the prediction of cerebral- and cardiovascular events during a 20 years follow-up period in an asymptomatic population of middle-aged subjects.

**Methods:** We evaluated 529 asymptomatic persons through a prospective study. Study population was divided into two subgroups: patients with and without MetS. Echo-color-Doppler was used in order to assess the presence of subclinical atherosclerotic diseases. A 20 years follow-up study was carried out in order to estimate the incidence of cerebral- and cardiovascular, fatal and non fatal, events (AMI, stroke, abdominal aneurysm, TIA, angioplasty).
Results: 242 cerebro- and cardiovascular events were registered, 43 fatal (24 in MetS and 19 in controls) and 199 non fatal (120 with MetS and 79 without it, p<0.0001). Free-events survival was lower in patients suffering from MetS (p<0.0012; HR 0.687; CI 95%: 0.5274-0.8889). Ultrasound showed a higher prevalence of subclinical atherosclerosis in patients with MetS than in the unafflicted ones (68.12% vs. 57.5% p=0.01; OR = 1.58 with CI 95% = 1.10-2.28, p<0.01).

Conclusions: Patients with MetS have a higher cardiovascular risk that can be explained by atherosclerotic changes: the components of MetS interact to affect both macro- and microangiographically and promote the development of subclinical atherosclerosis. So we recommend to prevent the development of MetS abnormalities and to investigate the presence of subclinical atherosclerosis by echo-color-Doppler in order to stratify more accurately the global CV risk.

P2304 | SPOTLIGHT
Metabolic syndrome is associated with and predicted by resting heart rate: cross-sectional and longitudinal findings from Kailuan study
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Background: Although higher resting heart rate (RHR) has emerged as a predictor of transitioning atherosclerosis, the precise mechanisms remain obscure. This present investigation was to test whether there was a positive relationship between RHR and metabolic syndrome (MetS) and whether RHR was a predictor of future metabolic syndrome.

Methods and results: A large vocational cohort (Kailuan Study) was surveyed in 2006-2007 and some were followed-up longitudinally. MetS was diagnosed when a participant presented at least 3 of the following: abdominal adiposity, low HDL cholesterol, high triglycerides, hypertension, and impaired fasting glucose. RHR was derived from ECG recording. Firstly, a clear and positive association between RHR and MetS was found in a cohort of 89 860 participants recruited in 2006-2007: the odds ratio of having MetS was 1.49 (95% confidence interval, 1.32-1.69) in subjects with RHR at 95-104 beats/minute than at 55-64 (reference) after adjusting for age, sex, education, cigarette smoking, alcohol drinking, physical activities, BMI, hypertension, diabetes and hyperlipidemia, inflammation marker and renal function. Secondly, during 4 years follow-up of 43,725 individuals who could not presented predictive value for CAD. 1,5-AG may be superior to HbA1c in predicting CAD in non-diabetic population.

Conclusion: The findings suggest that subgroups of the population in many countries in Europe still consume I-TF in amounts that increase their risk of coronary heart disease. Under current EU legislation, the sale of products containing I-TF is legal but conflicts with the WHO recommendation to minimise the intake of I-TF. A EU-legislatice limit on I-TF in foods is an effective strategy to achieve this goal.

P2305 | BEDSIDE
Predictive value of 1.5-amyloido-gluc for prevalence of coronary artery disease in non-diabetic adults
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Purpose: Elevation of glycated hemoglobin (HbA1c) level is predictive of the prevalence of coronary artery disease (CAD) and mortality. Serum 1.5-amylodo-gluc (1.5-AG) levels rapidly decrease concomitantly with the excretion of glucose in urine. Serum 1.5-AG is a useful clinical marker for short-term glycemic control and lived in Leningrad after the Siege. Relative telomere lengths were measured on Hitachi-902. Control group of age and sex matched subjects (n=47, 67-84 years) was born in the other parts of USSR with no exposure to severe famine and lived in Leningrad after the Siege. Relative telomere lengths were measured by quantitative PCR and the ratio of telomere repeat copy number to single gene copy number (T/S) was calculated for each DNA sample. Informed consent was obtained from all participants.

Results: Age differences between groups are not significant (p=0.24 according to Fisher criteria). Survivors of Siege of Leningrad had lower anthropometric data (height 162.4±1.7 vs 165.9±4.8 cm, p<0.007) and weight 72.5±14.9 vs 79.9 kg (p<0.002), higher systolic blood pressure (147±5.4 vs. 140±3.2 mmHg, p<0.008). There were no significant differences in the prevalence of cardiovascular disease in 2 groups: only prevalence of atrial fibrillation was slightly higher in the control group (8 (18.3%) vs 25 (8.2%), p=0.05).

Conclusions: Early life famine is associated with telomere shortening in both genders but not with cardiovascular diseases. Perhaps negative outcome after famine can be compromised by long-term post-siege period.

P2307 | SPOTLIGHT
Industrial trans fat in popular foods is still a health issue in europe: a market basket investigation
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Purpose: To minimise the intake of industrial trans fat (ITF) and thereby reduce the risk of coronary heart disease, nearly all European countries rely on food producers to voluntarily reduce the ITF content in food. The objective of this study was to investigate the efficiency of this strategy in 2012-2013 in 20 European countries.

Methods: The ITF content in pre-packaged biscuits/cakes/wafers was assessed in a market basket investigation. Three large supermarkets were visited in each capital, and in some countries, three additional ethnic shops were included. Results: A total of 596 samples of biscuits/cakes/wafers with “partially hydro-genated vegetable fat” or a similar term high on the list of ingredients were analysed. 312 products had more than 2% of fat as ITF, exceeding the legislatively determined ITF limit in Austria, Switzerland, Iceland, Norway, Hungary and Denmark; the average was 19%. In seven countries, no ITF was found, whereas nearly 50% in Eastern European countries had products with very high ITF content. The products in the remaining four countries had intermediate levels. Of the five countries that were examined using the same procedure in 2006, three had unchanged ITF levels in 2013, and two had lower levels. The 18 small ethnic shops examined in six Western European countries sold 83 products that contained an average of 23% of the fat as ITF; all imported from countries in South-eastern Europe. In Sweden, this type of imported food was also available in large supermarkets.

Conclusion: The findings suggest that subgroups of the population in many countries in Europe still consume I-TF in amounts that increase their risk of coronary heart disease. Under current EU legislation, the sale of products containing I-TF is legal but conflicts with the WHO recommendation to minimise the intake of I-TF. A EU-legislatice limit on I-TF in foods is an effective strategy to achieve this goal.
Malnutrition is a key prognostic factor in patients with heart failure (HF). Prevalence of HF with preserved ejection fraction (PEF) (defined as left ventricular ejection fraction ≥50%) has been increasing in parallel with the aging of the population. It is an obvious association between HF-PEF and hypertension, diabetes mellitus, and insulin resistance. However, association between malnutrition and clinical outcomes in patients with HF-PEF remains to be elucidated. Aims: We evaluated and controlled nutritional status score (CONUT), prognostic nutritional index (PNI), and geriatric nutritional risk index (GRNI) in 190 patients with HF-PEF (mean 69.9±11.6 years) admitted to our hospital. CONUT consists of serum albumin level and total cholesterol level, and total lymphocyte count. PNI consists of serum albumin level and total lymphocyte count. GRNI consists of serum albumin level and ratio of body weight to ideal body weight. Patients were prospectively followed with the endpoints being cardiovascular death or rehospitalization. There were 56 events including 14 deaths and 42 rehospitalizations during a median follow-up of 14.0 months. Patients with cardiac events showed higher CONUT score (6, IQR 3.5-8 vs. 2.0, P=0.001), lower PNI score (30.4, 27.3-36.1 vs. 38.9, 35.7-42.4, P<0.001), and lower GRNI score (84.9, 77.5-92.3 vs. 96.3, 90.8-102.7, P<0.001) compared with those without. The correlations between each nutritional index and clinical parameters were examined. CONUT score correlated with age, LVFE, and serum brain natriuretic peptide (BNP) level. PNI score correlated with age, LVFE, and serum BNP level. GRNI score correlated with age, LVFE, and serum BNP level. In Cox proportional hazards analysis, higher CONUT score was associated with age, gender, NYHA functional class, and lower left ventricular ejection fraction (LVEF) compared with those without. Total lymphocyte count, serum albumin, and total cholesterol level were lower in patients with cardiac events. As a result, patients with cardiac events showed higher CONUT score (6, IQR 3.5-8 vs. 2.0, P=0.001), lower PNI score (30.4, 27.3-36.1 vs. 38.9, 35.7-42.4, P<0.001), and lower GRNI score (84.9, 77.5-92.3 vs. 96.3, 90.8-102.7, P<0.001) compared with those without. The correlations between each nutritional index and clinical parameters were examined. CONUT score correlated with age, LVFE, and serum brain natriuretic peptide (BNP) level. PNI score correlated with age, LVFE, and serum BNP level. GRNI score correlated with age, LVFE, and serum BNP level. Kaplan-Meier analysis revealed a significantly higher cardiac event rate was observed in patients with malnutrition than those without.

Methods: Malnutrition was associated with unfavorable outcomes in patients with HF-PEF. Evaluating nutritional status may provide valuable prognostic information in patients with HF-PEF.

Conclusions: A controlled and supervised diet and the introduction of functional foods (olive oil, fish, nuts and vegetables) seemed to be able to improve endothelial function in overweight and obese subjects after a short (3 months) and medium (18 months) period.
than among low consumers, but it was significantly worse among high cheese consumers than among low consumers.

Conclusion: Consumers of fresh dairy products and consumers of cheese adopt different dietary patterns with varying intakes of simple sugars, fats, and sodium. Adherence to dietary recommendations is better among high consumers of FDP than among people with lower consumptions.

P2313 | BENCH

Chronic dietary supplementation with inorganic nitrate recovers age-related cardiac dysfunction

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Background and objectives: Ageing is the predominant risk factor for cardiovascular diseases and contributes to increased cardiovascular morbidity and mortality in the elderly. Cardiovascular functions are regulated by nitric oxide (NO). The micronutrient inorganic nitrate, abundant in our everyday diet, is a major source for calcium NO and has recently been shown to provide cardiovascular vascular function. We hypothesized that age-related cardiac functions could be improved by a chronic dietary nitrate supplementation in senescent mice.

Methods: A chronic dietary nitrate supplementation regimen was performed in young old and old wild-type mice for 7 weeks with age-matched saline controls. Age related myocardial diastolic function was assessed non-invasively via echocardiographic pulsed wave and tissue doppler (early and late mitral inflow and annulus velocity pattern, E/A and E′/A′, respectively) and in-vivo microtip catheterization technique. To elucidate the underlying impacts of dietary nitrate on cardiac functions we determined NO-species, cGMP levels and cGMP dependent protein kinase activity and applied noninvasive cardiac magnesium-enhanced MRI to study in-vivo calcium cycling.

Results: Aged mice displayed an abnormal cardiac diastolic pattern, which was reversed by dietary nitrate supplementation (meaning: E/A young 1.6±0.3 vs old 1.1±0.3 vs old nitrate 1.5±0.2, p<0.05 and E′/A′ young 1.4±0.2 vs old 0.8±0.1 vs old nitrate 1.3±0.5, p<0.05, end-diastolic pressure volume relationship young 0.9±0.1 vs old 0.15±0.03 vs old nitrate 0.10±0.02, p<0.05 and isovolumic relaxation constant tau young 5.1±1.2 vs old 9.1±1.27 vs old nitrate 5.6±1.7, p<0.05).

Mechanistically, dietary nitrate supplementation increased plasma nitrite content in old mice (young 1.3±0.6 μmol; old 0.8±0.5 μmol vs old nitrate 4.2±1.4 μmol, p<0.05), enhanced cGMP levels (younger 1444±66 fmol/mg protein, old 95±35 fmol/mg protein vs old nitrate 231±142 fmol/mg protein, p<0.05) and PKG activity in old mice (young 0.65±0.30 activity/mg protein, old 0.40±0.16 activity/mg protein vs old nitrate 1.1±0.5 activity/mg protein, p<0.05). This was substantiated by analysis in nitrate supplementation in mice (young 1.57±0.1 enhancement ratio; old 1.34±0.1 enhancement ratio vs old nitrate 1.61±0.1 enhancement ratio, p<0.05).

Conclusion: We observed an altered age-related myocardial dysfunction, which was reversed by dietary nitrate supplementation. Our findings provide insights into mechanisms that undermine the impact of dietary micronutrients to counteract cardiac aging.

P2314 | SPOTLIGHT

Cardiac safety of so called “energy drinks”

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Objective: Cardiac safety of so-called “energy drinks” has recently raised national awareness in France. They are consumed in millions in France and Europe. The purpose of our study was to review a consecutive group of patients with CAD submitted to PCI. ADA criteria were used to define diabetes (FPG >= 126 mg/dl and/or 2-h glucose >= 200 mg/dl) and pre-diabetes (FPG 100–125 mg/dl and/or 2-h glucose 140–199 mg/dl) and/or HbA1c 5.7–6.4%.

Results: 350 patients were included (mean age 61±11.5 years, 76% male). Taken together, OGTT and HbA1c identified 54 (15.4%) new cases of diabetes (DM) and 205 (58.6%) cases of pre-DM; only 91 (26.0%) patients had a normal glucose metabolism. Taken alone, HbA1c identified 21/54 new cases of DM (Sens 38.9%, NPV 90.0%, AUC ROC 0.78; Kappa 0.52, p<0.0001). As compared with 26/54 cases identified with FPG alone (Sens 48.1%, NPV 91.9%, AUC ROC 0.88; Kappa 0.61, p<0.0001) and 46/54 cases identified with 2-h glucose (Sens 85.2%, NPV 97.4%, AUC ROC 0.9; Kappa 0.9, p<0.0001), FPG+HbA1c (the strategy recommended in the new guidelines) only identified 37/54 patients with DM (Sens 68.5%, NPV 94.8%, Kappa 0.79, p<0.0001). Performing the FPG+HbA1c in only high risk for diabetes (adapted Framingham Diabetes Risk Score ≥12; n=123, 35.1% of the total population) identified 49/54 dts cases of DM (Sens 90.7%, NPV 98.3%, Kappa 0.94, p<0.0001). Performing the OGTT in all patients with pre-DM in the initial FPG+HbA1c evaluation (n=209; 59.7% of the total population) identified 51/54 dts cases (Sens 94.4%, NPV 99.0%, Kappa 0.97, p<0.0001).

Conclusion: Only using FPG and HbA1c, as recommended by the 2013 guidelines, would leave undiagnosed around 1/3 of new cases of DM in CAD patients. Performing an OGTT in all patients with pre-DM in the FPG+HbA1c evaluation (almost 2/3 of the patients) identifies the majority of patient with DM. Only routine use of OGTT and HbA1c identifies all patients with undiagnosed DM.
P2318 | BEDSIDE
Effect of gestational diabetes mellitus (GDM) on arterial stiffness
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Objective: Gestational diabetes mellitus (GDM) may be associated with cardiovascular diseases. However, the relation between aortic stiffness and GDM is not clear. The present study aims to assess the aortic stiffness parameters by comparing GDM with a healthy control group via transthoracic echocardiography. Methods: A cross-sectional study involving 62 pregnant women (33 with GDM and 29 with uncomplicated pregnancy as controls) during the third trimester. The aortic strain, aortic distensibility, and aortic stiffness values were measured via transthoracic echocardiography. The average systolic and diastolic measurements were calculated following three consecutive measurements.

Results: Data on age, blood pressure levels, heart rate, and basic echocardiography were similar in both groups. BMI was significantly higher in the GDM group (p < 0.01). Aortic strain and distensibility were significantly lower in the GDM group (p < 0.01). Aortic stiffness index was significantly higher in the GDM group (p < 0.01) (Table 1).

Table 1. Clinical characteristics and measurement of aortic elastic parameters in the gestational diabetes group and the control group

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Body mass index (kg/m²)</th>
<th>Aortic diastolic diameter (mm)</th>
<th>Aortic systolic diameter (mm)</th>
<th>LV diastolic diameter (mm)</th>
<th>LV systolic diameter (mm)</th>
<th>Aortic strain (%)</th>
<th>Distensibility (cm²/mm²)</th>
<th>Aortic stiffness index (mm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30.18±5.7</td>
<td>28.72±5.02</td>
<td>24.52±3.4</td>
<td>27.30±3.4</td>
<td>46.18±4.5</td>
<td>29.42±5.6</td>
<td>12.29±4.2</td>
<td>6.24±4.2</td>
<td>4.02±1.3</td>
</tr>
<tr>
<td>29.66±1.4</td>
<td>26.15±3.8</td>
<td>22.69±1.3</td>
<td>26.34±3.1</td>
<td>26.71±4.2</td>
<td>30.14±3.1</td>
<td>16.43±5.3</td>
<td>7.76±4.2</td>
<td>3.19±1.1</td>
</tr>
<tr>
<td>p-value</td>
<td>0.05</td>
<td>0.03</td>
<td>0.26</td>
<td>0.003</td>
<td>0.50</td>
<td>-0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Aortic stiffness parameters did not exhibit any significant difference between the insulin-receiving group and the diet-controlled GDM group. Postprandial glucose levels were positively correlated to the level of the aortic stiffness index (p < 0.04) and were negatively correlated with the level of aortic strain (p < 0.01) and distensibility (p < 0.03).

Conclusion: Aortic strain is increased in women with GDM compared to the control group. There is a correlation between postprandial glucose and arterial stiffness.

P2319 | BEDSIDE
Essential hypertension: when ingredients contain “a little more sugar”
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Background: Sustained hyperglycemia, even in the prediabetic range, is associated with endothelial dysfunction, vascular stiffness and adverse cardiovascular outcomes. Aim of our study was to explore the additive effects of impaired glycated-hemoglobin (HbA1c) on essential hypertension sequelae.

Methods: We studied 465 never treated, newly diagnosed, essential hypertensive patients stage I-III (mean age 52±13 years, 47% female), non-diabetic and without known cardiovascular disease. Evaluation of hypertension was performed according to ESH Guidelines. Traditional glycemic indices (fasting plasma glucose-FPG, HBA1c and 2h oral glucose tolerance-OGT) were performed in all patients. Euglycemic group (E) included patients with all the above glycemic indices normal (FPG<100 mg/dL = Hba1c<5.7% = OGT<140mg/dL), while impaired Hba1c group (IH) included patients with Hba1c in prediabetic range (5.7-6.4%).

Results: The mean values of HbA1c and FPG were higher in IH compared to E (140±16 vs. 120±17 mg/dL, p<0.05 for all). However, IH presented higher prevalence of diastolic dysfunction (76% vs. 58%, p < 0.008), c-f PWV (12 vs. 4.9, p < 0.01) and were negatively correlated with the level of aortic strain (p < 0.01) (Table 1). Aortic strain and distensibility were significantly lower in the IH group than in the E group (p < 0.001). Aortic stiffness index was not significantly different between the two groups (p > 0.05). However, IH presented higher prevalence of metabolic syndrome (80.5% vs. 26.1%, p < 0.001), while they didn’t differ regarding gender (males 48.4% vs. 50.6%, p=0.723), BMI (28.5±4 vs. 29.5±4 kg/m², p=0.133), waist and hip circumference, waist to hip ratio and prevalence of abdominal obesity (p > 0.05 for all). With the only exception of the family history of cardiovascular disease (54% vs. 41%, p=0.004), the two groups didn’t differ significantly regarding classical cardiovascular risk factors, including office and 24hr blood pressure and heart rate (p > 0.05 for all). However, IH presented higher prevalence of diastolic dysfunction (54% vs. 41%, p=0.004), higher prevalence of metabolic syndrome (80.5% vs. 26.1%, p < 0.001), and lower TDI Em/Am (0.89±0.2 vs. 1.0±0.4, p=0.007), while they didn’t differ regarding LVMI, carotid IMT, ankle-brachial index, ACR and Aix (p > 0.05 for all).

Conclusion: In essential hypertension, presence of impaired Hba1c augments arterial stiffness, carotid atherosclerosis and left ventricular diastolic dysfunction. Compared to anthropometric measures, preperitoneal and fat thicknesses represents more sensitive indices of impaired glycated-hemoglobin.

P2320 | BEDSIDE
Exaggerated insulin secretion is a risk of hypoglycemia in patients with cardiovascular disease
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Purpose: Recently, hypoglycemia is suggested to induce the cardiovascular disease and endothelial cell dysfunction through increasing the platelet aggregation as well as the catecholamine secretion. However, characteristics of glycemic and insulin secretion profile in patients with hypoglycemia are still unknown. Hereby, we have planned to clarify the characteristics of oral glucose tolerance test profile in heart disease patients with hypoglycemia during OGTT.

Methods: Four hundred eighteen consecutive patients without known diabetes mellitus (66:11 y.o., 284 male) who admitted in order to detect the coronary artery disease during April 2006 to June 2013 were enrolled. Cine-angiography and 75G OGTT were performed. Fasting hypoglycemia was defined as blood glucose below 80 mg/dL at fasting blood glucose. Patients were classified into two groups (Group H and Group N) due to the existence of hypoglycemia.

Results: Hypoglycemia occurred in 24 patients (6.8%). Fasting blood glucose was lower (<0.001) in Group H (76±2mg/dL) than that in Group N (98±12 mg/dL), although Hba1c was similar (5.8±0.3 vs. 5.9±0.5%, n.s.). As for the insulin resistance, HOMA-IR of both groups was almost within normal value although it was lower in Group H (0.88±0.44) than in Group N (1.51±0.94, p = 0.001). HOMA-β in Group H was greater than that in Group N (135.6±7.40 vs. 68.3±3.99, respectively, p < 0.001). The accuracy of HOMA-IR and HOMA-β to predict fasting blood hypoglycemia were moderate. A receiver operating characteristic analysis (ROC) found that HOMA-IR had an area under the curve (AUC) of 0.74 (95%CI: 0.65-0.83) (<0.001) and HOMA-β had an AUC of 0.83 (95%CI: 0.73-0.92) (p < 0.001).

Conclusions: Patients with exaggerated insulin secretion tend to induce fasting blood hypoglycemia.

P2321 | BEDSIDE
Effects of dipetidyl peptidase-4 inhibitor and alpha-glucosidase inhibitor on left ventricular diastolic dysfunction in type 2 diabetes: results of 3D trial
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Background: Left ventricular (LV) diastolic dysfunction is frequently observed in patients with type 2 diabetes. Dipetidyl peptidase-4 inhibitor (DPP-4i) attenuates postprandial hyperglycemia (PPH) and may have cardio-protective effects. We compared the effects of the DPP-4i, sitagliptin, and the alpha-glucosidase inhibitor, voglibose, on LV diastolic function in patients with type 2 diabetes.

Methods: We conducted a prospective, randomized, open-label, multicenter study, and recruited diabetic patients with LV diastolic dysfunction. Patients received sitagliptin (30mg/day) or voglibose (0.6mg/day). The primary endpoints were changes in e’ and E/e’ ratio from baseline to 6-month later. The secondary efficacy measures included glucose, Hba1c, GLP-1, lipid profiles, oxidative stress markers and inflammatory markers.

Conclusions: Patients with exaggerated insulin secretion tend to induce fasting blood hypoglycemia.
Results: Study was completed in 40 patients in the sitagliptin group and 40 patients in the voglibose group. There was a significant increase in GLP-1 level between baseline and 24 weeks after in sitagliptin group (4.8±4.7 vs. 7.3±6.5, p<0.05). A decrease in HbA1c and body weight were significantly greater in sitagliptin group (-0.7±0.6 vs. -0.3±0.4, p<0.005, -1.3±3.2 vs. 0.4±1.8, p<0.05). There were no significant changes in e’ velocity and E/e’ ratio from baseline to 6-month later in both groups.

Analysis of covariance demonstrated that pioglitazone use is an independent factor associated with changes in e’ and E/e’ ratio. Among those without the use of pioglitazone, e’ increases and E/e’ ratio decreases in both sitagliptin and voglibose groups.

Conclusions: Our trial showed that sitagliptin reduces HbA1c greater than voglibose, but that both were not associated with improvement in echocardiographic parameters of LV diastolic function in type 2 diabetic patients.

P2322 | BEDSIDE
Determinants of left ventricular hypertrophy and diastolic function: role of obesity
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The role of obesity in left ventricular (LV) hypertrophy and diastolic function is not clear and the effect of hemodynamic and hormonal environment must be reconsidered.

Objective: To establish the influence of obesity in the presence of LV hypertrophy and in diastolic function.

Methods: 125 consecutive morbidly obese patients referred for bariatric surgery and 67 normal weight volunteers underwent transthoracic echocardiography. Adipokines, inflammation and and metabolic profile were determined. Logistic and regression analysis were performed for hypertrophy and diastolic function determinants, respectively.

Results: Hypertrophy was determined by obesity and hypertension (table). Diastolic function was determined by hypertrophy, adipokines and inflammatory circulating markers. Proinflammatory and proinflammatory factors had an independent direct effect on E/e’ ratio whereas anti-inflammatory factors had an independent indirect effect on E/e’ ratio.

Table 1

<table>
<thead>
<tr>
<th>Hypertrophy</th>
<th>Odds ratio</th>
<th>Confidence interval (95%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>12.29</td>
<td>2.48–60.75</td>
<td>0.007</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.86</td>
<td>0.91–8.95</td>
<td>0.07</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diastolic function**</th>
<th>Change in E/e’ ratio</th>
<th>Confidence interval (95%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophy**</td>
<td>12.29</td>
<td>2.48–60.75</td>
<td>0.007</td>
</tr>
<tr>
<td>Lepitin</td>
<td>0.12</td>
<td>0.07–0.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.08</td>
<td>-0.02–0.16</td>
<td>0.05</td>
</tr>
<tr>
<td>IL-10</td>
<td>-0.02</td>
<td>-0.04–0.03</td>
<td>0.02</td>
</tr>
<tr>
<td>TNF-α</td>
<td>0.09</td>
<td>-0.02–0.16</td>
<td>0.01</td>
</tr>
<tr>
<td>GLP-1</td>
<td>-0.07</td>
<td>-0.14–0.12</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Variables in the model: Obesity, hypertension, sex, HOMA, adiponecines.

Conclusions: Obesity is a strong independent factor for left ventricular hypertrophy but it does not have an independent influence on diastolic function. Diastolic dysfunction is determined by ventricular hypertrophy, lepitin and inflammation circulating markers.

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P2323 | BEDSIDE
General and regional adiposity as determinants of cardiovascular risk
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Objective: The present study sought to compare the various obesity measures as predictors of dyslipidemia, dysglycemia and essential hypertension.

Design and methods: A total of 1140 consecutive, non-diabetic subjects (51±13 years, 49% males) were studied. Body mass index (BMI), body fat content (FAT, using a portable bioelectric impedance body composition analyzer), waist (WC) and hip (HC) circumference and waist-to-hip circumference ratio (WHR) were measured/calculated. Visceral (V), perirenal (R) and mesenteric (M) fat thicknesses were also measured using a linear ultrasound probe.

Results: The prevalence of dyslipidemia, dysglycemia and essential hypertension was 88.1%, 44.2% and 67.2%, respectively. The prevalence of 0, 1, 2 or all 3 dysmictic conditions was 3.1%, 22.3%, 43.5% and 31.1%, respectively. Compared to patients with 1 and 2, patients with all 3 dysmictic conditions were predominantly male (39% vs. 45% vs. 66%, p<0.001), older (50±14 vs. 51±12 vs. 55±12 years, p<0.001), with higher BMI (27±4 vs. 28±5 vs. 29±5 kg/m², p<0.001), FAT (32±8% vs. 34±8% vs. 35±7%, p<0.004), WC (90±13 vs. 93±13 vs. 98±13 cm, p<0.001), HC (103±10 vs. 105±10 vs. 107±9 cm, p<0.001), WHR (1.0±0.08 vs. 1.0±0.09 vs. 1.0±0.11, p<0.001). V (57±24 vs. 62±24 vs. 72±26 cm, p<0.001), R (10±4 vs. 11±4 vs. 13±5 mm, p<0.001) and M fat (11±4 vs. 12±4 vs. 13±5 mm, p<0.001). All the obesity markers significantly (p<0.001) discriminated subjects with all 3 dysmictic conditions except (p=0.082), WHR and WC had the highest area under the curve followed by BMI, V, R and M and FAT (Table).

Table 1

<table>
<thead>
<tr>
<th>Area under the curve</th>
<th>95% Confidence interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist-to-hip ratio</td>
<td>0.627</td>
<td>0.585–0.669</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.623</td>
<td>0.581–0.665</td>
</tr>
<tr>
<td>V fat</td>
<td>0.575</td>
<td>0.492–0.665</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.599</td>
<td>0.557–0.642</td>
</tr>
<tr>
<td>Perirenal fat</td>
<td>0.594</td>
<td>0.546–0.641</td>
</tr>
<tr>
<td>M fat</td>
<td>0.592</td>
<td>0.546–0.638</td>
</tr>
<tr>
<td>Body fat content</td>
<td>0.573</td>
<td>0.492–0.654</td>
</tr>
</tbody>
</table>

Conclusions: Among the various obesity markers, WHR, WC and visceral fat emerge as the most significant determinants of dysmictic diseases while measures of total body fat (i.e. BMI and FAI) have less predictive power.

P2324 | BEDSIDE
Average daily heart rate, smoking and overweight: is there connection?
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Background: High average heart rate (HR) may lead to progression of coronary artery disease, poor course of heart failure and it also decreases expected life duration. However, the influence of smoking and overweight on average HR remains poor investigated in healthy young people.

Aim: The aims of the study were to estimate how overweight or smoking influences on average daily heart rate in young people and to reveal possible cumulative effect of both these conditions on HR.

Methods: We included 675 medical students into study, 277 men and 398 women were among them. Each person completed standard questionnaire concerning lifestyle, diet, smoking and underwent the measurement of the height, weight and calculation of the body mass index (BMI). The four groups were separated from the total cohort. Non-smokers with normal weight (BMI=22.8±2.1 kg/m²) formed the 1st group. The second one consists of overweight non-smokers (BMI=27.7±1.9 kg/m²). The third group includes smokers with normal weight (BMI=20.4±2.4 kg/m²). Overweight smokers (BMI=27.3±2.2 kg/m²) were enrolled into 4th group. The size of all groups was the same (n=31) in order to increase the sensitivity of the statistical criteria. Daily electrocardiogram (ECG) monitoring was performed to all subjects in 4 groups.

Results: The average daily HR was higher in case of overweight (82.8±4.1 vs. 73.5±3.9, p<0.005) and smoking (83.6±5.4 vs. 73.5±3.9, p=0.028). The average daily HR was also higher in group of overweight non-smokers than in nonsmokers with normal weight (84.5±4.8 vs 73.5±3.9, p=0.027). However, HR in case of isolated smoking, isolated overweight or combination of both these conditions was almost the same. The possible explanations of the received data are the follow, smoking leads to increasing of the level of noradrenaline in plasma and therefore cause a high HR. Overweight is connected with higher average HR due to poor physical form.

Conclusion: The overweight and smoking increases average HR itself. There are no cumulative effect of these two conditions on average HR. Young people that smoke, have excessive weight or both need to be closely followed in order to diminish cardiovascular risk in future.
Methods: Echocardiography was performed in 226 children aged 6 to 15 years (BMI 18 to 34 kg/m²). Left ventricular (LV) end-diastolic volume, LV mass, transmi-
tral peak flow velocity (E), and mitral annular myocardial velocity (Em) were mea-
sured. LV mass/volume ratio was calculated. Stroke volume (SV) was measured using aortic diameter and pulsed Doppler velocity profile. SV was indexed for body surface area (SVI). Effective arterial elastance (EA) was estimated by end-systolic pressure/SVI. End-systolic elastance (Ees) was calculated by a modified single-
beat method using systolic and diastolic blood pressure, SV, EF, timing intervals, and an estimated normalized ventricular elastance at arterial end diastole. High sensitive C-reactive protein (hs-CRP), fasting glucose, insulin, and homeostasis model assessment for insulin resistance (HOMA-IR) were also assessed.

Results: EA and Ees increased significantly with BMI (r=0.29 and 0.18, p<0.01, respectively). Arterial-ventricular coupling (Ea/Ees ratio) did not change with BMI. LV mass/volume ratio was positively associated with increased BMI (r=0.45, p<0.01). There were significant relationships between BMI and fasting glucose (r=0.14, p<0.05), insulin (r=0.51, p<0.01), HOMA-IR (r=0.52, p<0.01), and hs-
CRP (r=0.24, p<0.01). Ea, Ees, and LV mass/volume ratio correlated significantly with insulin (r=0.23, p<0.01, and 0.32, p<0.01, respectively) and HOMA-IR (r=0.22, 0.17, and 0.28, p<0.01, respectively). No significant relationships were observed between LV mass/volume ratio and arterial-ventricular stiffness and hs-CRP.

Conclusions: Obesity-related insulin resistance associated with combined arterial-ventricular stiffening may contribute to the increased prevalence of later cardiovascular diseases.

P2329 | BEDSIDE
Early onset of androgenetic alopecia is related with target organ damage in hypertension
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Purpose: The relationship between androgenetic alopecia (AGA) and essential hypertension is under investigation. The purpose of the present study is the evalu-
ation of the relationship between LV bioclinical damages due to hypertension with the presence and severity of androgenetic alopecia in untreated young male hypertens-
tives with early AGA onset.

Methods: We performed a cross sectional study in 62 newly diagnosed and un-
treated young male hypertensives with early AGA onset.

Conclusions: Our data reveal that miR-9 and miR-126 are closely related to essential hypertension in humans, as they show a distinct expression profile in hypertensive patients relative to healthy individuals and they are associated with clinical prognostic indices of hypertensive target organ damage in hypertensive patients. Thus, they may possibly represent potential biomarkers and candidate therapeutic targets in essential hypertension.

P2330 | BEDSIDE
Serum uric acid and left ventricular hypertrophy in Nigerian patients with essential hypertension
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Background: Hypertension is a cause of left ventricular hypertrophy (LVH), an independent cardiovascular risk factor. Although serum uric acid is elevated in hyperuricaemic, it plays a role in the development of LVH in non-hyperuricaemic hypertensive patients. In our setting, the identification of a relatively inexpensive risk marker like uric acid may be beneficial in directing more targeted cardiac investigations.

Objective: To assess the relationship between serum uric acid and LVH in un-
treated patients with essential hypertension.

Methods: A cross-sectional study was carried out in one hundred and thirty (85 females, 45 males) newly diagnosed untreated patients with essential hyperten-
sion in the out-patient clinics of our university. Sixty-five healthy age and sex matched non-hyperuricaemic hypertensive patients served as controls for comparison. Left ventricular hypertrophy was evaluated by trans thoracic echocardiography. Blood samples were collected for assessing uric acid levels.

Results: Hyperuricaemia was present in 46.9% and 16.9% of cases and con-

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trols respectively (p<0.001). Mean serum uric acid was significantly higher among the patients with hypertension (379.7±109.2 μmol/l) compared to controls (296.9±89.8 μmol/l; p<0.001). Left ventricular hypertrophy was present in 55.4% of the cases and 10.8% of the controls (p<0.001) and the commonest geometric pattern among the cases was concentric hypertrophy while the majority of the controls had normal left ventricular geometry. Among the hypertensive patients, LVH was commoner in the hypertensive patients with hyperuricaemia compared to those with normal serum uric acid levels (70.5% versus 42.0%, p<0.001). There was a significant linear relationship between mean uric acid levels and the left ventricular mass index (r=0.336, p<0.001). In regression analysis, uric acid was a significant independent predictor of left ventricular hypertrophy (β=0.246, p<0.003).

Conclusion: These results indicate that serum uric acid is associated with the presence of LVH in patients with hypertension even at the time of diagnosis, thus is a reliable marker of cardiovascular risk in this patient population.

P2331 | BEDSIDE
The association of central hemodynamics and serum markers with cardiovascular disease in Japanese men
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Purpose: Recently, arterial stiffness, central hemodynamics, and serum markers of cardiovascular damages [high-sensitivity cardiac troponin T (hs-cTnT) and N-terminal-proBNP (NT-proBNP)] have been much focused as biomarkers of predictor of cardiovascular morbidity and mortality in the general population.

Aim: The present study was conducted to examine the association of these markers with cardiovascular disease in Japanese men having annual health checkup.

Methods: hs-cTnT, NT-proBNP, some blood data and anthropometric parameters including radial augmentation index (rAI), brachial-ankle pulse wave velocity (baPWV), were obtained in 1427 Japanese male subjects coming to health check-ups. We defined brain and cardiovascular diseases as subjects having past history of cerebro-cardiac disease, and subjects treating now for cerebro-cardiovascular disease.

Results: In this study subjects, the hs-cTnT (≧0.09ng/ml) was detected in 4.1% (59 subjects). The subjects having cerebro-cardiovascular disease were 3.0% (43 subjects). The area under the receiver operator characteristic curve for hs-cTnT, NT-proBNP, baPWV, and rAI were 0.514, 0.618, 0.651, and 0.673 (95%CI: 0.425-0.604, 0.522-0.715, 0.563-0.740, and 0.585-0.761, respectively). Logistic regression analysis demonstrated that NT-proBNP (Odds ratio = 1.7, 95%CI: 1.3-2.7) (p<0.001) and rAI (Odds ratio 1.7, 95%CI: 1.1-2.8) (p<0.03), but not hs-cTnT (p=0.930) and baPWV (p=0.574), were significant variable to identify cardiovascular disease after the adjustment of confounding variables.

Conclusion: The central hemodynamics and NT-proBNP may be independent markers for the screening of cardiovascular disease in middle-aged health Japanese men. However, the hs-cTnT may not be useful for the screening of cardiovascular disease in these subjects.
Home blood pressure measurement (HBPM) + telemonitoring (TLM) in patients with chronic kidney disease (CKD) in a care program: a pilot study

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Methods: 931 treated hypertensive Pts were included during the first visit: 347 (37.27%) males, 584 (62.73%) females. After a mean follow-up of 12 months (6-20 months) 263 (28.25%) of the initially recruited Pts went through a follow-up evaluation: 178 females (30.48% of all recruited females), 85 males (24.49% of all recruited males). The mean age was 65.9±10.00 years. We gathered full medical history, physical examination, laboratory screening, echocardiography, intima-media thickness, office and home measured blood pressure, ambulatory blood pressure monitoring, Montreal Cognitive Assessment and Mini Mental State Examination. All the Pts were on combination treatment. SPSS 19 was used for the statistical analysis.

Results: 198 (21.26%) of the Pts had only one cardio-vascular risk factor – hyperton- laster. The largest number 394 (42.32%) of Pts were those who had ≥3 cardio-vascular risk factors. 209 (22.94%) were smokers, 488 (54.28%) had dys-

Conclusions: Among the patients with suboptimal home-measured blood pressure (71.44%) of the Pts were with high and very high SCORE result (for high-risk cardio-vascular risk factors. 209 (22.94%) were smokers, 488 (54.28%) had dys-

P2337 | BEDSIDE
Arterial stiffness is associated with left ventricular geometry and diastolic dysfunction in the elderly

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Purpose: Increased arterial stiffness is reported to be associated with left ventricular hypertrophy (LVH) and LV diastolic dysfunction. However, the impact of arterial stiffness on LV geometry including concentric LVH, eccentric LVH and concentric remodeling and on the interplay between LV geometry and LV diastolic function has not been fully elucidated.

Methods: 431 subjects (mean 70 years, 57% men, 41% diabetes mellitus) were evaluated after exclusion of patients with coronary artery disease, severe valvu- lar disease, cardiomyopathy and LV ejection fraction <50%. The brachial-ankle pulse wave velocity (baPWV), a marker of arterial stiffness, was measured using a Rapid BP Laboratory MnSDP-2 apparatus. For comparison, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), systolic blood pressure, diastolic blood pressure and mean arterial pressure were measured. For baPWV measurement were performed using BPLab® MnSDP-2 apparatus. For baPWV and baPWV + TLM revealed 4 (26%) pa- tients with white coat hypertension. After an average of 2 TLM sessions and 4.7 months, mean baPWV was 133/37 mmHg (fig). This BP amelioration could be realised without increasing the amount of pills (change type of medication, com- bination therapy). Most of the GP’s consider HBPM+TLM as an added value if additional support by the home program (patient education and report- ing) and feedback by the nephrologist is available. Patients experience TLM as a better follow-up (faster evaluation of results and adaptation of medication by GP).

Results: Average age of the patients’ 75 years. Mean eGFR (MDRD):28 ml/min/1.73 m². Mean BP: 151/74 mmHg. HBPM + TLM revealed 4 (26%) pa-
tients with white coat hypertension. After an average of 2 TLM sessions and 4.7 months, mean baPWV was 133/37 mmHg (fig). This BP amelioration could be realised without increasing the amount of pills (change type of medication, com-

Fig. 1. Change in mean SBP and DBP.

Conclusions: HBPM + TLM results in better and faster BP control. TLM is an added value but support of both patient and GP is essential.

P2337 | BEDSIDE
Arterial blood pressure monitoring and arterial stiffness values in patients with arterial hypertension with chronic obstructive pulmonary disease

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Purpose: The aim of the study was analysis of arterial blood pressure monitoring (ABPM) data and arterial rigidity (AR) values in patients with arterial hypertension (AH) with chronic obstructive pulmonary disease (COPD) in different stage of disease.

Methods: The study included 58 male patients with AH and COPD. Mean age was 63.3±8.9 years. There were 1st degree of AH in 6 patients, 19 patients had 2nd degree of AH and 3rd degree of AH was determined in 33 patients. Duration of disease was 5±5.2 years for AH and 7.7±5.9 years for COPD. All patients were divided into three groups. There were 18 patients with moderate COPD, 21 patients with severe COPD and 19 patients with very severe obstruction. All three groups were comparable with the general parameters of the examined patients. Comparison group included 50 male patients with essential AH without chronic respiratory diseases. Control group included 22 healthy male individuals. Compar- ison group subjects were comparable with examined patients on age sex di-

Fig. 1. Change in mean SBP and DBP.

Conclusions: HBPM + TLM results in better and faster BP control. TLM is an added value but support of both patient and GP is essential.

Figure 1. Change in mean SBP and DBP.

Conclusions: Increased arterial stiffness influence LV geometry as well as the interplay between LV geometry and LV diastolic dysfunction in the elderly.

LV geometry, arterial stiffness and LVDD.

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Figure 1. Change in mean SBP and DBP.

Conclusions: HBPM + TLM results in better and faster BP control. TLM is an added value but support of both patient and GP is essential.

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Figure 1. Change in mean SBP and DBP.

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Figure 1. Change in mean SBP and DBP.

Conclusions: HBPM + TLM results in better and faster BP control. TLM is an added value but support of both patient and GP is essential.
during daytime value. There is prevalence of abnormal AIx during 24-hour monitoring.

Conclusion: Pronounced increasing of AI is most common in patients with severe and very severe COPD. There is trend of rising ABPM readings in patients with COPD combined with AH as with normal and increased rigidity. We observed circadian variations of AR parameters with prevalence of nocturnal abnormality. Thus it is reasonable perform 24-hour ABPM on patients with AH and COPD.

TARGET ORGAN DAMAGE IN HYPERTENSION II

P2339 | BEDSIDE
The role of metabolic syndrome and the ventricular geometry The evaluation of TOD in hypertension study
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Background: The cardiac effects of hypertension include a variety of structural changes such as increases in left ventricular mass (LVM). But little information is available on the importance of the metabolic syndrome which induce different left ventricular geometry patterns.

Purpose: To assess the prevalence of left ventricular geometry patterns in a large selected hypertensive population with verified Metabolic Syndrome and included in METHOD Study (Metabolic Syndrome Target of Hypertension Organ Damage Study), an observational ongoing registry of hypertension-related target organ damage (TOD), were considered for this analysis.

Methods: A total of 2404 untreated and treated essential hypertensives consecutively attending, for the first time, our hospital outpatient hypertension clinic and included in METHOD Study (Metabolic Syndrome Target of Hypertension Organ Damage Study), an observational ongoing registry of hypertension-related target organ damage (TOD), were considered for this analysis.

Results: Eccentric Hypertrophy pattern was present in 672 (27.95%) patients, Concentric Hypertrophy pattern in 965 patients (40.14%) and Concentric remodelling pattern in 405 (16.85%) patients. Compared with 362 (15.06%) patients with normal left ventricle geometry, those with eccentric or concentric hypertrophy as well as those with concentric remodelling were the more older, more frequently overweight, had higher systolic blood pressure as well as uric acid levels and included a greater proportion of subjects with diabetes hyperlipidemia and renal impairment (Creatinine levels>1.4 in males or >1.2 in females). The prevalence of hypertriglyceridemia was similar in patients with normal geometry and those with concentric remodelling.

According to a logistic regression analysis, fasting blood glucose >7.0 mmol/l, renal impairment, systolic and diastolic blood pressure, age and female sex were the main independent predictors of eccentric hypertrophy pattern.

Finally independent predictors of concentric remodelling were fasting blood glucose >7.0 mmol/l, Female Sex and Systolic Blood Pressure

Conclusions: Hyperglycemia, age and female sex component of metabolic syndrome seems to be the major factors in the development eccentric hypertrophy pattern. These results suggest that metabolic syndrome may contribute to the development of concentric hypertrophy. Hyperlipidaemia and hyperuricemia play an important role in development concentric hypertrophy.

P2340 | BEDSIDE
The influence of arterial hypertension on the initiation and progression of atrial fibrillation
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Purpose: To determine the influence of arterial hypertension (AH) on the course of various forms of atrial fibrillation (AF).

Methods: 87 patients were examined (42 men and 45 women, mean age 49±8.2 years). Patients were divided into 4 groups according to the type of AF and the presence of AH: 1 - with paroxysmal AF (AFp) + AH (22 patients); 2 - with persistent AF (AFp) + AH (23 patients), 3 - with AFp without hypertension (20 patients), 4 - AFp without hypertension (22 patients). The data of daily electrocardiogram monitoring (DECGM) and daily blood pressure monitoring (DBPM) were evaluated.

Results: It was found, that patients with AFp +AH and AFp+AH had significantly higher systolic blood pressure variability (SBPV) and diastolic blood pressure variability (DBPV) than patients with AF without hypertension (SBPV, mm Hg: 16.1±7.1, 11.3 respectively (p<0.05); DBPV, mm Hg: 13.6±1.3, 9.2±1.1 respectively (p<0.05)). The blood pressure load (a "pressure-time" index for systolic and diastolic blood pressure) was raised from 43% to 68% in patients of groups 1 and 2 respectively, compared to 9% and 15% of patients in groups 3 and 4 respectively.

A significant increase of the number of patients with AFp compared with AFp was detected along with the increase of the duration of hypertension by 21,3±3,5 months (1,325; 95%; confidence interval 1,126 – 1,557; p<0.01).

Conclusion: The presence of arterial hypertension contributes to the more severe course of atrial fibrillation. The increased indices of daily blood pressure monitoring raise the frequency and duration of atrial fibrillation paroxysms and promote the development of persistent atrial fibrillation.

P2341 | BEDSIDE
Assessment of arterial stiffness with an easy method in preeclamptic patients
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Background: Arterial stiffness is the term used to define the rigidity of arterial walls. Arterial stiffness and its hemodynamic results have been shown to be associated with increased cardiovascular morbidity and mortality in previous studies. Women with a history of pre-eclampsia in past pregnancies have a higher risk of developing cardiovascular disease later in life. In this study, we aimed to assess the arterial stiffness with a noninvasive and easily applicable oscillometric method in pregnant women and with and without preeclampsia.

Methods: Ninety pregnant patients with a mean age of 30.7±6.5 years were included in the study. Patients were divided into two groups based on the presence of pre-eclampsia. Vascular measurements were performed with a Mobi-O-Graph 24-h PWV Monitor, an automatic oscillometric device.

Results: All of vascular function parameters were significantly higher in the patients with pre-eclampsia. In the pre-eclampsia group the PWV value was positively correlated with gestational age, maternal age, glucose, creatinine, augmentation index and central blood pressure. In linear regression analysis, the PWV value was found to be positively correlated with gestational age, maternal age and central systolic blood pressure. In women with severe pre-eclampsia had significantly higher blood pressures, PWV, AIx and cardiac output in comparison to mild pre-eclampsia.

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pearson's correlation coefficient</th>
<th>Linear regression coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>p value</td>
<td>Value</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>0.357</td>
<td>0.016</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>0.631</td>
<td>0.001</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>0.342</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.437</td>
<td>0.003</td>
</tr>
<tr>
<td>Augmentation index (%)</td>
<td>0.349</td>
<td>0.019</td>
</tr>
<tr>
<td>Central diastolic blood pressure (mmHg)</td>
<td>0.689</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Oscilometric PWV measurement is generally accepted as the most reproducible, rapid, easily applicable and low-cost non-invasive method for the assessment of large artery stiffness and it may contribute to estimation of future cardiovascular risk profiles of patients admitted with pre-eclampsia.

P2342 | BEDSIDE
Diurnal systolic blood pressure load relates with aortic stiffness in patients with newly diagnosed arterial hypertension with dipping status
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Background: Blood pressure (BP) load, defined as the percentage of abnormally elevated BP readings, is usually provided on the report of ambulatory BP monitoring. The relationship between blood pressure load, independently from blood pressure level, and target organ damage in hypertension disease is under discussion. Aortic stiffness is considered valuable index of subclinical damage in hypertensive patients offering to cardiovascular risk estimation. We aimed to explore the relationship between diurnal systolic blood pressure load and aortic stiffness in patients with newly diagnosed essential hypertension regarding their dipping status.

Methods: We studied 218 patients with newly diagnosed and never treated essential hypertension (mean age 51±11 years, 189 males). We performed: a. 24h ambulatory blood pressure measurement (ABPM) in order to measure blood pressure load and estimate dipping status and b. carotid-femoral artery pulse wave velocity (PWV) in order to evaluate aortic stiffness. We divided total population in Group A (n=156, dippers) and Group B (n=82, non-dippers).

Results: No significant differences were found within groups regarding PWV, BPM systolic and diastolic BP in office and ABPM, BPM systolic BP in office pulse pressure, diurnal BP systolic load. However, Group A patients were younger with decreased 24h pulse pressure had increased systolic and diastolic blood pressure and pulse pressure in office and 24h ABPM measurements. In Group A, diurnal BP systolic load was related with indices of aortic stiffness: PWV (r=0.21, p<0.01), pulse pressure (r=0.24, p<0.01) and 24h pulse pressure (r=0.51, p<0.001). No such relationship was found in Group B patients. In a multivariate regression analysis, where systolic BP (office or ABPM), pulse pressure (office or ABPM) and mean
BP were inserted as independent variables. PWV was associated with aortic stiffness indices in dipper untreated hypertensive patients, but not independently of BP level. The significance of this index regarding arterial stiffness is lost in hypertensive patients with non-dipping status, where different pathophysiological mechanisms are present leading to a more augmented 24h blood pressure load.

P2343 | BEDSIDE
Extreme dipping as an independent predictor of left ventricular hypertrophy
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Purpose: Development of left ventricular hypertrophy (L VH) is a multifactorial and incompletely understood process. Aim of our study was to determine the effect of blood pressure’s (BP) circadian abnormalities on L VH.

Methods: We studied 780 consecutively newly diagnosed, never treated, non-diabetic, hypertensive patients stage I (51±13 years old, 45.3% females). Echocardiographic left ventricular mass calculation was performed from parasternal long axis and normalized for height in meters to the power of 2.7 (LVM). Established cutoffs (<49 for males and <45 g/m2 for females), the study population was split in group with normal (n=649) and increased LVM (n=131). Dipping status was defined according to day-night SAP circadian variation from 24 hour ambulatory blood pressure monitoring.

Results: Patients with L VH were older (54±13 vs 51±13, p=0.018), while there was no difference regarding gender (43.7 vs 45.8, p=0.88). Prevalence of dippers was higher in patients with no L VH (50% vs. 35.6%), while there was no difference in the prevalence of non-dippers between the two groups (34.2 vs. 35.6). Moreover, prevalence of extreme dippers and reverse dippers was higher in patients with L VH (18.6% vs. 9.3% and 10.2% vs. 6.5%). Logistic regression analysis revealed that, compared to dippers, extreme dippers had 2.9 higher odds (95% CI: 1.5-5.5, p=0.001) of L VH, independent of age, gender and body mass index, while reverse and non-dippers had no significant difference (OR: 1.8, 95% CI: 0.8-4.0, p=0.122 and OR: 1.3, 95% CI: 0.8-2.3, p=0.315, respectively).

Conclusion: Extreme dipping status is an independent predictor of left ventricular hypertrophy.

P2344 | BEDSIDE
Early morning blood pressure, pulse wave velocity, central aortic Pressure and predictive risk factors of Ischemic Stroke in masked hypertensive patients
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Objectives: The clinical significance of early morning hypertension (EMHT) is not still somewhat clear. We evaluated the prevalence of masked early morning or nocturnal hypertension (NHT) and effects of arterial stiffness, pulse wave velocity (PWV) and wave reflections on central aortic pressure (CAP) in hypertensive patients with ischemic stroke (IS).

Methods: We analyzed a total 450 hypertensive patients with IS, investigate masked hypertension (MHT) using 24hr ambulatory blood pressure monitoring (ABPM). Among the MHT, classified as masked EMHT (early morning BP ≥135/85 mmHg and night-time BP ≤120/70 mmHg), Masked NHT (Daytime BP ≤135/85 mmHg and night-time BP >120/70 mmHg) and using radial artery applanation tonometry, aortic pulse analysis was performed in MHT.

Results: 128 patients was observed MHT with ischemic stroke. EMHT was found in 55.6% of MHT patients (n=71). Compared with patients both with EMHT and NHT, EMHT had higher aortic pulse wave velocity (PWV) and augmentation index (AI) and AI75 (AI to HR 75 beat/min), ASP (Central aortic systolic pressure) and pulse pressure were also higher in the EMHT.

Conclusion: Our results suggest that higher prevalence of masked EMHT. A significant increase of early morning BP, especially systolic BP, might be predictive risk factor of ischemic stroke events rather than nocturnal BP. Hence ASP measurement might be particularly important for the early detection of ischemic stroke event.

P2346 | BEDSIDE
Influence of gender on mortality and perioperative outcomes in patients undergoing transcatheter aortic valve implantation: insights from the FRANCE 2 Registry
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Aim: Transcatheter aortic valve implantation (TAVI) is an alternative to surgical aortic valve replacement in high risk patients, avoiding the risks of thoracic surgery and extracorporeal circulation. The relative event rates following TAVI are not well described and seem to differ between genders. We sought to determine gender imbalances in TAVI patients in regard of baseline presentation, management, and prognosis.

Methods and results: A total of 3972 patients underwent TAVI and were prospectively included in the FRANCE 2 registry. Women (n=1967) presented older age, lower rates of coronary artery disease, chronic obstructive pulmonary disease, renal failure and arrhythmia, but higher prevalence of hypertension and congestive heart failure (43.7% vs 39.7%; p=0.010). EuroSCORE was similar between genders. Women presented smaller aortic annulus sizes and were implanted with smaller bioprostheses.

Women presented higher rates of major bleedings and vascular events at one month. Men presented higher mortality rates than female (23.7% vs 19.3%; p=0.021). Female gender, NYHA class III or IV, transapical approach and moderate to severe preprocedural aortic regurgitation were independent predictors for one-month all-cause mortality. We found a specific interaction between gender and EuroSCORE that set EuroSCORE to be not discriminant in women to establish one-month mortality. Female gender was an independent predictor of one-year survival (HR 0.71 95%CI [0.57-0.88]).

Conclusions: Men and women presented many differences in baseline characteristics, procedural and clinical outcomes. Notably women presented an 18.5% decrease in one-year all-cause mortality compared to men but higher rates of major bleedings and vascular events. Not only actual predictive scores seem to be inconvenient to female TAVI patients, but specificities in procedural management of female patients should be studied further.

P2347 | BEDSIDE
Gender-specific differences and hospital outcomes in patients undergoing transcatheter aortic valve implantation and conventional surgery: results from the German aortic valve registry
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Background: Transcatheter aortic valve implantation (TAVI) appears to be an effective alternative to conventional aortic valve replacement (AVR) for the treatment of aortic stenosis in surgical high-risk patients. However, gender differences in patients treated with TAVI or conventional aortic valve replacement (AVR) have been poorly investigated.

Methods: From 2011 to 2012, 30,292 consecutive patients undergoing repair for aortic valve disease were prospectively enrolled into German Aortic Valve Registry (GARY). For the present analysis patients were divided into four categories: females treated with TAVI or AVR and males treated with TAVI or AVR.

Results: Female patients had a comparable general health status, but were older and more likely to be treated with TAVI than male patients (table). Among those with TAVI, concomitant coronary bypass surgery was more often performed in male patients (38.8 versus 28.2%). In the TAVI group the transfemoral access route was more frequently used among females (72.2 versus 63.3%). The rate of TIA/stroke was similar in all groups, but significant aortic regurgitation (>1+) and vascular complications were more often observed in the TAVI cohort. The incidence of in-hospital death was lowest in male patients with AVR, followed by female patients with AVR and both TAVI groups.
Conclusions: Female patients undergoing repair for aortic valve disease were older and more likely to be treated with TAVI in comparison to their male counterparts. In-hospital mortality was higher in female patients treated with AVR, whereas mortality rates were similar in both groups treated with TAVI.

P2348 | BEDSIDE
Influence of gender on outcome following Transcatheter Aortic Valve Implantation (TAVI): Meta-Analysis of the Literature
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Objectives: This study sought to undertake a comprehensive meta-analysis of studies investigating differences in outcome after Transcatheter Aortic Valve Implantation (TAVI) in women compared to men.

Background: Sex differences exist in pathogenesis, clinical presentation and outcome in aortic stenosis (AS). Still limited information is available concerning sex differences in periprocedural complications and outcome after TAVI.

Methods: PUBMED, MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials were screened. Inclusion criteria were: AS treated with all forms of TAVI; studies targeting specifically on sex/gender differences; and at least two of the following outcome data: 30-day all-cause mortality, all-cause mortality during follow-up (>3 months), major vascular complications, and major bleeding. Exclusion criteria were studies in which gender was merely considered in subgroup analysis.

Results: 11 observational studies with a total of 5867 patients (3087 women, 2780 men) were included. At 30 days (10 studies, 2716 women, 2438 men), female sex was associated with a significant, 25% lower mortality rate [odds ratio (95% confidence interval) = 0.75 (0.60-0.94)]. Nine studies with 4985 patients (2576 women, 2407 men) providing data on mortality during follow-up reported a significant survival advantage for women [0.67 (0.53-0.83)]. Whereas major vascular complication rate was greater in women (9 studies, 2757 women, 2536 men) [1.72 (1.39 to 2.14)], major bleedings (7 studies, 1977 women, 1899 men) were not significantly different between genders [1.12 (0.91, 1.37)].

Conclusions: There is evidence for a significant overall survival benefit in women over men treated with TAVI.

P2349 | BEDSIDE
Evaluation of the aortic valve and root with new automated quantitative 3-dimensional model in candidates for transcatheter aortic valve replacement

Background: Progress in the technique of transcatheter aortic valve replacement (TAVR) requires good knowledge of the aortic root. With this aim new specialized software appears with the ability of automated quantitative modelling of the aortic valve (AV) and root from 3D transesophageal echocardiography (3D TEE). The purpose of this study was to validate this model with the measurements made manually.

Methods: 21 patients (84.4±6.22 years, 66.7±6.22 females) undergoing TAVR in our center where included. The diameters and areas of the aortic annulus (AA), sinus of valsalva (SV) and sinotubular union (STU) were manually measured by 3D TEE. Afterwards, the images were analyzed using the new software (Figure 1).

Results: We found a moderate correlation and interobserver variability between the automated and manual measurements at the level of the AA: Intraclass correlation coefficient was 0.618 (0.227-0.838), (r: 0.635, p: 0.000), good correlation and interobserver variability for the SV area: ICC was 0.775 (0.495-0.910), (r: 0.778, p: 0.000) and moderate correlation for the STU area: ICC was 0.621 (0.231-0.839) (r: 0.630, p: 0.000).

Conclusions: Automated 3D quantification of the AV and aortic root is possible. There is a proper correlation between manual and automated measurements analyzed by the new model. The assistance in percutaneous techniques such as TAVR is one of the possibilities of this new software. Prospective studies are necessary to define its applicability.

P2350 | BEDSIDE
30-day interim analysis of transfemoral aortic valve implantation using a 29mm balloon expandable transcatheter heart valve: results from the SOURCE XT sub-registry
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Purpose: TAVI is an alternative treatment for high-risk patients with severe, symptomatic aortic stenosis. Screening examinations in first generation TAVI feasibility and post market studies confirmed the need for a valve size for patients with larger aortic annuli. A sub-registry of SOURCE XT was initiated for the 29mm SAPIEN XT transcatheter valve (THV) and next generation transfemoral delivery system (TF-DS) to collect post market data.

Methods: The multicenter, observational SOURCE XT sub-registry prospectively enrolled a mean of 105 patients receiving the size 29mm THV with the TF-DS through a 20Fr expandable introducer sheath. 30-day follow-up was 99% completed.

Results: The mean patient age was 80±6.7 years. The size 29mm THV was primarily implanted in male patients (93%), whose cardiac anatomy and body size supported a larger THV device. The mean Logistic EuroSCORE was 18.6±12.4% with the majority of patients in NYHA class III/IV (65.7%) at baseline. Hypercholesterolemia (96.2%), congestive heart failure (40.2%), diabetes mellitus (37.1%), renal insufficiency/failure (26.7%), cancer (25.7%), pulmonary hypertension (24.8%), prior CABG (20.0%), and history of stroke (13.3%). Device success was 95.8%. The incidence of VARC outcomes at 30-days was very low with major bleeding at 9.6%, life-threatening bleeding at 4.8%, major vascular complications at 5.8%, re-hospitalization at 4.9%, and stroke 1.9%. No myocardial infarction was observed and 9.6% required a new pacemaker implantation. Substantial functional improvement was seen at 30-days compared to baseline, with the majority of patients in NYHA class II (95.7%) and significantly better overall quality of life (ED-SQ, p<0.0001). Hemodynamic parameters, including mean gradient (8.7±3.2mmHg) and effective orifice area (2.1±0.4cm²) showed significant improvement to baseline (p<0.0001), with a remarkably low incidence of moderate and severe paravalvular leak (1.4%). Based on the current analysis, the overall survival at 30-days was 97.1%.

Conclusion: The 30-day interim analysis of the SOURCE XT transfemoral sub-registry demonstrates early safety and effectiveness of the size 29mm THV with high device success and is associated with a low incidence of mortality (2.9%), stroke, bleeding complications and re-hospitalizations, while demonstrating significantly improved patient functional capacity and hemodynamic performance with a very low incidence of moderate/severe PVL.

P2351 | BEDSIDE
Outcomes of TAVI in patients with severe aortic stenosis and large aortic annulus
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Purpose: To assess device safety, procedural success and early 30-days outcomes of the 31mm self-expanding transcatheter heart valve, in comparison with the other device sizes.

Methods: The study includes 76 consecutive patients who underwent transcatheter aortic valve implantation (TAVI) with 26mm self-expanding valve (n=21, 28%), 29mm (n=20, 26%) and 31mm (n=35, 46%).

Results: Patients with 31mm prosthesis were significantly younger (26mm: 83.6±7.0; 29mm: 85.5±7.3; 31mm: 79.8±8.0, p=0.001), prevalently males (26mm: 19%; 29mm: 40%; 31mm: 91%; p=0.00001) with higher STS scores (26mm: 21.1±5.6; 29mm: 20.1±16%; 31mm: 32.2±15%; p=0.01) and lower left ventricular ejection fraction (26mm: 53±17%; 29mm: 55±7.3; 31mm: 45±12%; p=0.04). A device success was obtained in 71 (93%) cases in the overall population, without significant differences between groups. 5 patients required acute valve-in-valve therapy. Procedural, fluoroscopy and revalving times and procedural outcomes did not differ. At discharge we observed similarly a significant reduction in transaortic mean gradient and increase in aortic valve area; the incidence of paraprosthetic regurgitation was significantly minor in 31mm valve when compared with 28mm. Paced rhythm at implantation, bicuspid valve and similar anatomy were similar. Time of hospitalization in CRS 31mm patients did not differ from the other groups and 30-days outcomes were similar.

Conclusions: The 31mm self-expanding transcatheter heart valve can be safely implanted in patients with complex aortic valve disease, large annuli, dilated left ventricles, severe aortic regurgitation and low annular calcifications.
Background: Aortic annulus diameter is critical information for transcatheter aortic valve replacement (TAVR). Because aortic annulus is of an oval shape, three-dimensional measurements are indispensable. However, the geometric change of aortic annulus after TAVR is unclear. Thus, we tried to evaluate the shape and size of aortic annulus before and after TAVR by three-dimensional transosophageal echocardiography (3D-TEE).

Methods: In 2027 patients (27 vs. 1.8 ± 1 y/o) patients with severe aortic stenosis undergoing TAVR with SAPIEN XT prosthesis (23mm or 26mm), 3D-TEE was performed before and after replacement. Some patients were enrolled in PREVAIL JAPAN study. We performed the off-line analysis of aortic annulus geometry by the dedicated software (O-LAB, Philips). We defined the aortic annulus as the plane formed by the 3 lowest points of aortic valve cusps and measured manually aortic annulus long diameter (DL), short diameter (DS) and Planimetry of the area (AAA) by multi-planar reconstruction images before replacement. Geometric mean diameter (DGM) was calculated as $\sqrt{\frac{2\cdot AAA}{\pi\cdot DL\cdot DS}}$. Noncircularity of aortic annulus was calculated as eccentricity index (INECC) $=\frac{1-(DS/DL)}{\%}$. After replacement, we also measured the external geometry of stent frame at the inflow annulus was calculated as eccentricity index (INECC) $=\frac{1-(DS/DL)}{\%}$. After replacement, we also measured the external geometry of stent frame at the inflow level in the same way.

Results: Aortic valve area (0.56 ± 0.12 vs. 1.36 ± 0.20 cm², p < 0.01) and mean pressure gradients (54.19 vs. 12.34 mmHg, p < 0.01) were improved after replacement. AAA (3.38 ± 0.69 vs. 3.66 ± 0.63 cm², p < 0.01) and DGM (20.7 ± 2.1 vs. 21.5 ± 1.8 mmH, p < 0.01) were significantly increased (0.86 ± 0.76 mmH and INECC decreased was (16.9 ± 6.1 vs. 28.2% ± 2%), p < 0.01) after replacement.

Conclusions: The replaced prosthetic valve was larger than aortic annulus before TAVR and the shape changed into aortic annulus. Should be three dimensionally measured in view of the geometric change after TAVR.

**Table 1. Baseline characteristics and clinical outcomes of patients that underwent TAVR**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Weight (kg/m²)</th>
<th>Normal weight</th>
<th>Overweight</th>
<th>Obese</th>
<th>Morbidly obese</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>85.6±6.3</td>
<td>86.5±6.4</td>
<td>84.9±6.4</td>
<td>80.7±6.8</td>
<td>76.8±7.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>STS score (%)</td>
<td>12.9±3.9</td>
<td>11.9±3.5</td>
<td>11.1±3.6</td>
<td>10.8±3.7</td>
<td>10.8±3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>96±103</td>
<td>116±117</td>
<td>110±117</td>
<td>86±103</td>
<td>58±89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>9.2% ± 7.7</td>
<td>4.6% ± 4.1</td>
<td>9.3% ± 7.7</td>
<td>0.9% ± 0.7</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>1-year mortality</td>
<td>33.2% ± 25.6</td>
<td>21% ± 17.1</td>
<td>17.6% ± 17.6</td>
<td>0.001</td>
<td>6MWT: 6-minute walk test.</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** In patients with severe AS undergoing TAVR, those having obesity had better survival than those with normal body weight, after adjustment for different baseline characteristics. The "obesity paradox" was evident in high-risk AS patients across different treatment modalities.

P2353 | BEDSIDE

**Influence of body-mass-index on survival of aortic stenosis patients treated by transcatheter vs. surgical valve replacement or medical therapy only: Insights on obesity-paradox from the PARTNER trial**

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Purpose: To evaluate possible influence of body mass index (BMI) on survival of patients with severe aortic stenosis (AS) in different treatment strategies. Methods: Patients who underwent transcatheter aortic valve replacement (TAVR) in the PARTNER trial were evaluated according to their BMI (n=2,519): underweight (<18.5 kg/m², n=97), normal weight (18.5-25 kg/m², n=1,029), overweight (25-30 kg/m², n=800), obese (30-40 kg/m², n=484), morbidly obese (>40 kg/m², n=97). In addition, outcomes of patients treated by surgical valve replacement (SAVR, n=287) or medical management only (MM, n=177) were evaluated according to their BMI.

Results: In the total group of patients that underwent TAVR: obese patients were younger, had lower STS score and worse 6-minute walk performance at baseline (table). Patients that were underweight and those with morbid obesity had the highest 30-day mortality. After propensity matching, adjusting for dissimilarity between the normal, overweight and obese groups, obese patients had lower 1-year mortality than patients with normal body weight (18.7% vs. 29.4%, p=0.002). Multivariate analysis revealed that obesity was a strong independent predictor for 1-year survival after TAVR: obesity vs. normal weight, odds ratio 1.37 (CI 1.05-1.78, p=0.02); obesity vs. underweight, odds ratio 2.13 (CI 1.4-3.22, p<0.001). In patients that underwent SAVR or MM, a trend towards lower 1-year mortality appeared in obese patients, compared to those with overweight and normal weight: SAVR, 19.2% vs. 26% vs. 25.7%; MM, 42.5% vs. 48.1% vs. 54.4%, respectively.

Conclusions: TAVR is associated with a continuous and sustained LVMi regression at one year. This finding suggests that TAVR is able to reverse the ventricular pathological changes induced by chronic pressure overload in high-risk elderly patients.

P2354 | BEDSIDE

**Left ventricular mass regression in high-risk aortic stenosis patients undergoing transcatheter aortic valve replacement**


Background: Left ventricular mass index (LVMi) regression is associated with improved outcome following surgical aortic stenosis treatment. However, it is presently unknown whether the LVMi regression occurs in elderly higher-risk individuals undergoing transcatheter aortic valve replacement (TAVR).

Methods: From a prospective cohort of patients undergoing TAVR we systematically collected echocardiographic data. Both left ventricular mass and the left atrium diameter index (LADI) were calculated during screening and post procedure, and at 30 days, six months and one year follow-up. Increased LVMi was defined as >115 g/m² in men, and >95 g/m² in women. Longitudinal LVMi and LADI changes over time were assessed through mixed models in patients with and without increased LVMi.

Results: The study included 311 patients (mean age: 83.8±8 years old). At baseline, 50% of patients had increased LVMi (mean±135±28 g/m²). These patients were more often females (57% vs. 39%; p=0.01), had more balloon valvuloplasty (41% vs. 23%; p<0.01), a lower left ventricular ejection fraction (53% ± 14 vs. 58% ± 10; p<0.01), and had an increased LADI (2.6±0.4 vs. 2.3±0.4; p<0.01) compared to patients with normal LVMi. A significant decrease in the LVMi occurred over time among patients with increased LVMi at baseline (p<0.0001 (Fig. 1).

Conclusions: TVAR is associated with a continuous and sustained LVMi regression at one year. This finding suggests that TAVR is able to reverse the ventricular pathological changes induced by chronic pressure overload in high-risk elderly patients.
P2356 | BEDSIDE
Effect of pressure unloading on myocardial remodelling in patients undergoing TAVI
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Objective: The regression of left ventricular hypertrophy (LVH) after aortic valve replacement (AVR) is a crucial indicator of LV pressure unloading. However, biochemical markers are currently established to reliably monitor LV mass regression after transcatheter aortic valve implantation (TAVI). Therefore, the objective of the present study was to investigate the time course and prognostic impact of serum biomarkers of extracellular matrix (ECM) remodelling over a 6 month period after TAVI.

Methods and results: In this study, thirty-two high-risk patients (81±1.5 years, female 59%, EuroSCORE 28.3±13.1%) underwent TAVI (transfemoral: n=24, 75%; transapical: n=8, 25%) for symptomatic, high-gradient AS (MPG 41±1.38 mmHg). In these patients, plasma levels of matrix metalloproteinase-9 (MMP-9), tissue inhibitor of metalloproteinases-1 (TIMP-1) and -4 (TIMP-4), growth differ-
entiation factor-15 (GDF-15), as well as two fetal molecular variants of Tenascin-C (B+ Tn-C and C+ Tn-C) were measured at baseline, at 1 week and at 1, 3 and 6 months after valve replacement.

During a 6-month follow-up period, LV mass index decreased in trend from 171.7±62.1g/m² to 140.9±57.6g/m² (p=0.06), LV ejection fraction increased from 50.1±19.9 to 59.0±14.2 (p<0.013). This was accompanied by an extensive ECM reorganization represented by significant increases of TIMP-1 (121.1±43.3 vs. 140.1±40.0, p=0.008), TIMP-4 (3120.4±1335.9 vs. 3805.2±1525.1, p=0.001) and GDF-15 (2295.6±1209.9 vs. 2967.8±1379.2, p=0.005) serum levels. In con-
trast, plasma levels of MMP-9 (92.3±150.9 vs. 57.1±36.4; p=0.51) and C+ Tn-C (35.9±22.2 vs. 32.5±13.4; p=0.001) decreased.

During 6 month follow-up, the structural changes of the myocardium were accom-
plished by a functional improvement with a significant increase in 6 min-walk distance from 148.1±113.0 to 192.9±122.6 (p=0.036). The number of patients in NYHA class <2 increased from 6.3% (n=2) before to 78% (n=25; p<0.001) after TAVI.

Conclusion: Pressure unloading after TAVI results in mid-term LV mass index reduction and functional improvement, which are accompanied by a complex structural and functional re-organisation of the cardiac ECM. The changes in the serum levels of ECM presented in this study likely reflect reverse remodelling with a switch from a high matrix turnover in disease-associated active tissue remodeling, to physiological cardiac tissue homeostasis after TAVI.

COMPILATIONS AFTER TAVI

P2358 | SPOTLIGHT
First degree atrioventricular block is associated with increased risk of atrial fibrillation and heart failure in patients with aortic stenosis: the SEAS study
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ification, the independence was specifically maintained with a more severe AF (HR: 4.0 [95%CI: 0.8-0.8 m/s in PM group and 4.1±0.8 m/s in controls; p=ns).

P2359 | BEDSIDE
Incidence of prosthetic valve endocarditis at patients after TAVI
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Transcatheter percutaneous aortic valve implantation is a new technique for aor-
tic valve stenosis and regurgitation. Because of short time of usage we are still
have not all information about follow-up of this group of patients. Some studies
suggests that up to 20% of patients after TAVI dies because of infection compli-
cations, however the information about incidence of prosthetic valve endocarditis (PVE) is limited.

The aim of the study was analysis of series of 129 patients after TAVI between 03/2010 and 03/2014. At 63% of patients Medtronic Corevalve was implanted, at
35% Edwards Sapien XT and at 2%, Medtronic Engager. In 73% cases trans-
femoral access was used, in 15% direct aorta, in 8% subclavian and 4% apical.
44% of patients have implanted 29 mm bioprosthesis, 42% - 26 mm, 23 mm 8% and
and 6 mm 3%. In one year follow up we found 3 patients who met the diagnostic criteria valve endocarditis. The first patient had endocarditis on native mitral valve as a com-
plication of severe pneumonia but TAVI prothesis was not infected (26 mm Corevalve). The second patient had endocarditis on right atrium catheter during six months due to AF antagulation complications, however the Edwards Sapien XT 29 mm had no signs on PVE. At third patient we observed typical PVE on Medtronic Corevalve 29 mm due to urosepsis. Only the first patient survived (33%), the sec-
d due to non-cardiological complication of transplantation, the third dies due to PVE complications.

 Infective endocarditis after TAVI is rather rare complication (2%), and not always
the bioprosthes implanted by TAVI procedure is affected by PVE. However in cases of PVE of TAVI implanted valve we found 100% of mortality.

P2360 | BEDSIDE
Impact of permanent pacemaker implantation on left ventricular function and outcome of patients with aortic valve stenosis

Background: Aortic stenosis (AS) is the most common valve disease nowadays with an increasing prevalence, especially in elderly population. In these patients, coexisting degeneration of the electrical conduction system, leading to sick sinus syndrome or advanced atrioventricular block, requiring implantation of permanent pacemaker (PM), is commonly encountered. Very little information, however, is available in literature on the impact of PM implantation on the natural history of patients with asymptomatic AS.

Methods: From our Valve Disease Registry (1989-2013), we identified 59 pa-
ients (52 males, age 75±9 years), with asymptomatic moderate or severe AS (mean jet aortic velocity 3.4±0.8 m/s, mean ejection fraction 56±9%), that re-
quired permanent right ventricular PM implantation. All patients in sinus rhythm on baseline ECGs in the SEAS study of PVE of TAVI implanted valve we found 100% of mortality.

Results: The mean follow-up period was 41±3.3 years for the PM group and
4.2±2 years for the control group (p<ns). There was not significant difference in the mean progression of the severity of AS (last jet aortic velocity 4.0±0.8 m/s in PM group and 4.1±0.8 m/s in controls; p=ns). On the contrary, mean ejection frac-
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tion was significantly lower at the last follow-up in PM group (48.8±10% vs 53.9%, p =0.001). Furthermore, patients in PM group had major clinical events (death or aortic valve replacement) in 74.6% of cases vs 57.6% of controls (p =0.027).

Conclusions: Right ventricular pacing plays an unfavourable role on left ventricular function and outcome of patients with AS. Our findings suggest that these patients should be followed-up more closely or biventricular pacing should be considered in selected cases.

P2361 | BEDSIDE
Mortality in patients requiring pacemaker implantation following transcatheter aortic valve replacement: Insights from a systematic review and meta-analysis

Purpose: While the incidence of permanent pacemaker (PPM) implantation following transcatheter aortic valve replacement (TAVR) has been established, the effect of PPM implantation on mortality is less well described. Thus, we performed a meta-analysis to determine the impact of PPM following TAVR on all-cause mortality.

Methods: PubMed and Cochrane CENTRAL were searched for studies reporting outcomes in patients that underwent PPM implantation following TAVR. Primary end-point was all-cause mortality. Summary effect estimates were generated with random-effects modeling to compare all-cause mortality between patients requiring PPM and patients not requiring PPM.

Results: 193 studies were identified in total to PPM implantation after TAVR were assessed at the full-text level. We abstracted data from 7 published studies. Among the 7 included studies, all-cause mortality data during follow-up was available on 534 patients that received PPM implantation following TAVR compared with 470 patients that did not receive PPM implantation. As seen in the figure, requirement of PPM implantation following TAVR did not increase all-cause mortality during follow-up compared with patients that did not require PPM implantation following TAVR (pooled odds-ratio: 1.00 [95% CI 0.78-1.27], p =1.00).

Conclusions: Our current meta-analysis suggests that the need for PPM following TAVR does not increase the risk of all-cause mortality. Further studies directed towards changes in left ventricular function, cost, length of stay, valve type and post-pacemaker complications should shed light on the overall effect of PPM implantation in patients following TAVR.

P2362 | BEDSIDE
Left bundle branch block after transcatheter aortic valve implantation: 1-year prognostic significance
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Purpose: Conflicting results are reported about the prognostic impact of left bundle-branch block (LBBB) after transcatheter aortic valve implantation (TAVI). We sought to evaluate the 1-year prognostic significance of new and persistent LBBB post-TAVI using the CoreValve Revalving System.

Methods: In our center 98 patients underwent TAVI implantation for severe symptomatic aortic stenosis (valve area <1.0cm²; all transfemoral approach, but 3 subclavian approach). Three patients who died within 24 h for major procedural complications (1 cardiac tamponade, 1 life-threatening arrhythmia, 1 failure of TAVI), and 2 patients who died within 7 days precluding the acquisition of persistent LBBB on ECG (1 stroke; 1 lung failure; 1 irreversible shock) were excluded from the analysis. All complications were evaluated according to Valve Academic Research Consortium definition.

Results: Among 92 patients, 34 (37%) (group A) developed a new and persistent LBBB and the remaining 58 (group B) did not. At baseline logistic EuroSCORE (17.8±11.6 vs. 20.9±15.8, P=0.27) and septal wall thickness (14.3±1.7 mm vs. 14.8±1.9 mm, P=0.778) were not different between group A and B. After TAVI with similar markers of myocardial damage (peak troponin 3.8±4.9 μg/l vs 4.5±8.2 μg/l, P=0.38) and peak white blood cells: 11.6±6.4±10⁹/l vs. 12.7±7.2±10⁹/l, P=0.342), a higher rate of advanced atrio-ventricular block (AVB) was found in group A vs. group B (50% vs. 22.4%, P<0.001). The LBBB plus AVB was strongly correlated with permanent pacemaker implantation (PP) (P=0.001) and an even higher rate of PPI was found in group A (56% vs. 19%, P<0.0001). At 1-year the recovery of left ventricular (LV) ejection fraction (EF) was similar between group A and B (baseline to 1-year: EF 2.6±3.8% vs. 4.2±8.3%, P=0.379); 10 patients died (8 for non-cardiac cause) and 9 were hospitalized for heart failure (HF): (5 (14.7%) events occurred in group A (P=0.281). By adjusted Cox analysis the development of acute kidney injury (AKI) and the EuroSCORE were associated with a poor outcome (all cause mortality and HF) (HR 5.96, 95% CI 2.08 to 17.11, P =0.0001; HR 1.50, 95% CI 1.006 to 1.966, P=0.025, respectively), but not the development of LBBB (P=0.279).

Conclusions: After TAVI, 34% of patients developed a new and persistent LBBB without marker of more advanced myocardial damage or inflammation. LBBB was associated with a higher rate of 30-days PPI, without impairment of recovery of LV systolic function. The development of AKI, rather than LBBB, increases the risk of mortality and HF hospitalization at 1-year.

P2363 | BEDSIDE
Predictors of permanent pacemaker implantation after transcatheter aortic valve implantation with the Medtronic CoreValve system

Background: High-grade conduction disturbances (CD) requiring permanent pacemaker (PPM) implantation (impl) occur in up to 34% of patients (pts) following transcatheter aortic valve implantation (TAVI) with the Medtronic CoreValve (MCV).

Objective: To provide knowledge of possible predictors that might help to decrease the rate of PPM impl.

Methods: From July 2010 until June 2012 in total 198 pts with high surgical risk underwent transcatheter aortic valve implantation with the MCV system (26/29/31mm). Pts (23) with pre-existing PPI or bifascicular block were excluded from the study leaving 175 pts for retrospectively evaluation for ECG, anatomical, and procedural predictors for PPM impl. To evaluate procedural data, device position was measured on fluoroscopy as distance between the proximal aspect of the MCV stent frame below the native aortic annulus.

Results: We analyzed 175 pts (mean age 79.8±6.05 years, log Euroscore 24.2±0.8, mean pressure gradient 44.2±1.04 mmHg, AWA 0.65±0.01 cm², LVEF 50.6±0.8%). A total of 42 (24%) pts underwent MCV-impl post TAVI. 19 (10.9%) pts showed pre-operative CD, including first degree AV block, right (RBBB) and left bundle branch block (LBBB). Pts with PPM impl showed a significantly longer pre-procedural PQ interval versus pts without PPM-impl (201.3±8.9 ms versus 175.7±4.3 ms, P=0.04).

Pre-existing LBBB was not associated with PPM impl. There was no pt with a pre-existing LBBB in the MPM group (PPM versus no-PPM: 0 versus 9.8%). Pre existing RBBB showed a slightly enhanced trend in the MPM group but was not statistically significant (16.7% versus 5.2%; P=0.05).

The depth of the device impl showed also no significant difference (PPM versus no-PPM: 12.2±0.38 mm versus 11.6±0.21 mm; P=0.17), but was only associated with a new onset LBBB. LBBB group versus non-LBBB group: 20.9±1.29, 95% median 19.50 to 20.307mm versus 11.15±0.316mm, P=0.05. The overall rate of new post-procedural LBBB was 38.9%.

In a multivariate logistic regression analysis for predictors of post-interventional PPM impl including pre-PQ time, pre-existing RBBB, pre-existing LBBB, fibrillation and depth of implantation, only pre-PQ time interval turned out as independent predictor for PPM impl.

Conclusions: Only a prolonged pre-PQ time interval turned out as independent predictor for PPM impl after TAVI. The implantation depth of the CoreValve was not associated with PPM implantation but with a new-onset LBBB after TAVI.

P2364 | BEDSIDE
Impact of left ventricular conduction defect with or without need for permanent right ventricular pacing on functional and clinical recovery after TAVR

Background: Left ventricular conduction disturbances (VCD) are relatively common after transcatheter aortic valve replacement (TAVR). Previous publications show different impact of left bundle-branch block (LBBB) with or without need for permanent pacemaker implantation (PM) on survival. Effects on patients’ functional outcome is still unclear.

Methods and results: 212 patients (Age 80.8±6.4 years, logEuroscore 28.95 ±10.8, MVR 64.1%) underwent TAVR with use of the CoreValve prosthesis. Follow-up (FU) included clinical examination and standardized echocardiography. After TAVR 125 (59%) patients showed VCD, whereof 41 (19%) patients were implanted with new PM, 33 (16%) had preexisting PM, and 48 (23%) showed new LBBB with intrinsic AV conduction.

After 9 months FU the presence of VCD was associated with less improvement of left ventricular ejection fraction (LVEF) (LVEFbaseline=54±15.9%, LVEF5months=51±15.9%, P=0.08) if compared to patients without VCD (LVEFbaseline=54±15.9%, LVEF5months=51±15.9%, P=0.01). Only the presence of PM was associated with higher functional NYHA classes (p =0.05), and higher levels of NT-proBNP (p =0.05), when compared to patients without VCD or patients with LBBB alone. 20.4% of PM patients remained in NYHA class ≥3 after TAVR.
as compared to 5.3% without VCD and 4.7% with LBBB (p = 0.001). Independent predictors for all-cause mortality were aortic regurgitation index (p = 0.001), a higher EuroSCORE (p = 0.01), and impaired LVEF (p = 0.04).

Conclusion: The occurrence of VCD is common after TAVR and is associated with unfavorable left ventricular functional recovery. The combination of both VCD and unfavorable RV pacings has adverse impact on heart failure related symptoms after TAVR.

P2365 | BEDSIDE Impact of TAVI on primary hemostasis disorders T. Caspar1, D. Desprez2, L. Grunebaum2, H. Same1, A. Trinh1, H. Petit-Eisenmann1, L. Jesel1, M. Kindo3, P. Ohlmann1, O. Morel1, 1University Hospital of Strasbourg, Department of Cardiology, Strasbourg, France; 2University Hospital of Strasbourg, Laboratory of Hematology, Strasbourg, France; 3University Hospital of Strasbourg, Department of Cardiovascular Surgery, Strasbourg, France

Purpose: Aortic valve stenosis (AVS) can be complicated by bleeding associated with primary hemostasis disorders. These latures include acquired type 2A von Willebrand syndrome which is a deficiency of high molecular weight multimers of von Willebrand factor (vWF), due to increased proteolysis of vWF through the atherosclerotic valve. The association of AVS and gastrointestinal bleeding (GIB) from angiodysplasia is defined as Heyde’s syndrome. It is unclear yet if the beneficial effect of surgical valve replacement on this disorders is applicable to patients undergoing transcatheter aortic valve implantation (TAVI).

Methods: From November 2012 to December 2013, we prospectively enrolled 49 consecutive patients with severe AVS addressed for TAVI in our institution. Bleeding complications and transfusion needs were evaluated. Biological primary hemostasis parameters (with analysis of vWF) were assessed at baseline and one day after the procedure.

Results: The mean age was 84 years and 55% were male. Mean logistic euSCORE was 31.9%. 9 patients (18.4%) had history of GIB or noninvestigated anemia, with 1 (2%) Heyde’s syndrome. Both commercially available pros-thetic valves were used. Thirty-day mortality was 8.3%. 20 patients (41.7%) had bleeding complications (9 life-threatening bleedings (18.8%), 9 major bleedings (18.8%), 2 minor bleedings (4.2%). There was no fatal bleeding, and no GIB was observed. 24 patients (50%) were transfused with red blood cells (RBC) during hospitalization, 89 units of RBC were transfused in total (1.85 units per patient). Hemoglobin level was lower one week after TAVI compared to before the procedure (10.18 vs 11.59 g/dl, p < 0.05). There was a significant increase at one week of vWF antigen, vWF activity (Ristocetin Colator), and vWF collagen-binding activity, consistent with the improvement of primary hemostatic abnormalities involving vWF.

Conclusions: Bleeding complications are frequent in patients with AVS undergoing TAVI, and possibly linked to primary hemostasis abnormalities involving vWF. These abnormalities are significantly improved after TAVI. Moreover, our observations, although limited to a small single-center study, suggest that the fact of Heyde’s syndrome can be cured by TAVI.

P2366 | BEDSIDE Importance of complete coverage of all major aortic arch cerebral arteries with a novel neuro-deflection device in patients undergoing TAVR: Results from the DEFLECT I study A. Baumbach1, M. Mullen2, A. Brickman3, P. Margolis4, J. Kovac5, D. Hildick-Smith1, C. Pietras6, C. P. Ohlmann1, O. Morel1, 1University Hospital of Strasbourg, Department of Cardiology, Strasbourg, France; 2University Hospital of Strasbourg, Laboratory of Hematology, Strasbourg, France; 3University Hospital of Strasbourg, Department of Cardiovascular Surgery, Strasbourg, France

Purpose: Aortic valve stenosis (AVS) can be complicated by bleeding associated with primary hemostasis disorders. These latures include acquired type 2A von Willebrand syndrome which is a deficiency of high molecular weight multimers of von Willebrand factor (vWF), due to increased proteolysis of vWF through the atherosclerotic valve. The association of AVS and gastrointestinal bleeding (GIB) from angiodysplasia is defined as Heyde’s syndrome. It is unclear yet if the beneficial effect of surgical valve replacement on this disorders is applicable to patients undergoing transcatheter aortic valve implantation (TAVI).

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Conclusions: Bleeding complications are frequent in patients with AVS undergoing TAVI, and possibly linked to primary hemostasis abnormalities involving vWF. These abnormalities are significantly improved after TAVI. Moreover, our observations, although limited to a small single-center study, suggest that the fact of Heyde’s syndrome can be cured by TAVI.

P2367 | BEDSIDE Feasibility and exploratory efficacy evaluation of the embrella embolic deflector system for the prevention of cerebral emboli in patients undergoing transcatheter aortic valve implantation J. Rodes Cabau1, P. Kahler2, F. J. Neu mann3, G. Schymik4, J. Webb5, T. Lefèvre6, M. Schlammn7, M. Thomas8, F. Beyersdorf9, A. Vahanian9, 1Bristol Heart Institute, Bristol, United Kingdom; 2University of Edinburgh, Edinburgh, Scotland; 3University of Cincinnati College of Medicine, Cincinnati, Ohio, USA; 4University of Bern, Bern, Switzerland; 5University of Bristol, Bristol, United Kingdom; 6University of Strasbourg, Department of Cardiovascular Surgery, Strasbourg, France; 7University of Strasbourg, Laboratory of Hematology, Strasbourg, France; 8University Hospital of Strasbourg, Department of Cardiovascular Surgery, Strasbourg, France; 9Global Institute for Research, Richmond, United States of America

Methods: This pilot study included 52 patients who underwent transfemoral TAVI with the SAPIEN XT valve. The EED system was used in 41 patients; while 11 patients underwent TAVI without embolic protection (control group). The occurrence of cerebral microembolization was monitored during the entire TAVI procedure by transcranial Doppler (TCD), and cerebral DW-MRI examinations were performed at baseline, within 7 days and at 30 days following TAVI.

Results: The EED system was successfully deployed at the level of the aortic arch in all patients with no complications. The deployment of the EED system was associated with a lower lesion volume compared to the control group (30[20-50] mm3 vs. 50[30-70] mm3, P<0.003). All new cerebral lesions had disappeared at the DW-MRI performed at 30 days following TAVI. Two strokes unrelated to the EED device occurred at days 2 and 29 after TAVI.

Conclusions: This study showed the feasibility and safety of using the EED system in TAVI procedures. The EED system did not prevent the occurrence of cere-bral microemboli during TAVI procedure. However, the embolic protection system was associated with a reduction in lesion volume. Further studies are warranted to determine the efficacy of using the EED system during TAVI procedures.

P2368 | BEDSIDE High-on-treatment-platelet-reactivity in interventional valve procedures A. Polzin, M. Scheleicher, S. Attoh, V. Veulemanha, K. Hellhammer, T. Rühl, M. W. Menz, M. Kirm, T. Zeis, Department of Cardiology, Pneumology and Angiology, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Purpose: Since introduction of transcatheter aortic valve implantation (TAVI) and interventional clipping of the mitral valve, many patients with high surgical risk underwent those procedures. Major complications are ischemic events as well as the mean total volume of new ischemic brain lesions was lower after TAVR removal (0.90±0.12 cm3 vs. 0.22±0.12 cm3, p<0.01) and at TAVR completion (0.11±0.12 cm3 vs. 0.19±0.12 cm3, p=0.07). The mean total lesion volume with lesions with FC after TAVR removal than with IC (0.51±0.91 vs. 1.3±0.85 cm3, p<0.05). The mean total lesion volume was numerically lower with FC after TAVR completion than with IC (0.6±0.94 vs. 1.1±0.69, p=0.2).

Conclusions: This sub-analysis of the DEFLECT I study demonstrates that full coverage of all three cerebral aortic branches can reduce significantly the mean total volume of new ischemic brain lesions. The most significant reduction was seen when the positioning of the deflector was maintained until the TAVI device was removed. In the first report, the embolic protection during TAVI reduces larger volume embolic brain lesions.
Complications after TAVI / Imaging in aortic stenosis

**Results:** 62% of patients undergoing interventional valve procedure had clopidogrel HTPR. Aspirin antiplatelet effects were insufficient in 12% of patients. 22% of investigated patients had a VARC complication. The incidence of HTPR to clopidogrel as well as aspirin therapy did not differ between patients with- and without VARC- complications. Ischemic complications were observed in 3% of patients undergoing interventional valve procedures, bleeding complications in 22%. Clopidogrel and aspirin HTPR was not significantly higher in patients with ischemic complications in comparison to patients without ischemic complications (clopidogrel: 83% vs. 61%; p=0.26; aspirin: 33% vs. 19%; p=0.36). Furthermore, no significant differences existed between clopidogrel, respectively aspirin HTPR in patients with bleeding complications in comparison to patients without bleeding complications (clopidogrel: 58% vs. 71%; p=0.065; aspirin: 18% vs. 19%; p=0.83).

**Conclusion:** In conclusion, clopidogrel HTPR occurs in almost two-thirds of patients undergoing interventional valve repair. Future studies investigating optimal antiplatelet regimen after TAVI should consider the high incidence of clopidogrel HTPR and monitor clopidogrel antiplatelet effects carefully.

P2369 | BENCH

**TAVI failure: systematic appraisal of published data**

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1Galway University Hospital, Galway, Ireland; 2McGill Health University Hospital, Montreal, Canada; 3German Heart Center of Munich, Munich, Germany; 4CVPath Institute, Gaithersburg, United States of America

**Purpose:** Bioprosthetic surgical valve failure is well described, however no study has described transcatheter heart valve (THV) failure in a large series. We performed a systematic review of published literature to investigate the causes, diagnosis, management of THV PVE, valve thrombosis, and structural valve failure differed considerably from surgical bioprosthetic failure.

**Methods:** Between January 2002 and October 2013, all published studies reporting patient level data on THV failure were identified by systematic electronic search. Outcomes were defined according to the VARC criteria.

**Results:** Among 56 publications and 69 individual cases of THV failure, prosthetic valve endocarditis (PVE) (n=29), structural valve failure (n=8), and THV thrombosis (n=12) were identified. The microbiological profile of THV PVE was similar to that of surgical PVE, though up to 1/3 of patients underwent surgical intervention. THV thrombosis occurred at a mean 8±7 months post implantation and was successfully treated with anticoagulation in 2/3 of patients. Two novel causes of THV failure were identified: 13 cases of late THV embolization and 7 cases of THV compression following cardiopulmonary resuscitation. These failure modes have not been reported in surgical aortic valve replacement, and all involved balloon expandable THV systems. Potential risk factors for late THV embolization include THV undersizing/underexpansion; bicuspoid and non-calcified aortic valve; and asymmetric root calcification.

**Conclusions:** THVs are susceptible to failure modes typical of surgical bioprostheses and unique to the design of THVs. THV compression and late embolization represent complications previously unreported in the surgical literature. Management of THV PVE, valve thrombosis, and structural valve failure differed considerably from surgical bioprosthetic failure.

**P2373 | BENCH**

**Aortic annulus sizing strategy in TAVI: comparison of echocardiography and CT, impact on aortic regurgitation incidence and patient prognosis**


**Background:** Trans aortic valve implantation (TAVI) is an alternative to surgery in high-risk patients. The aim of this study was to evaluate the predictors of mortality in the TAVI registry of our institution.

**Methods:** 136 consecutive patients undergoing TAVI were included between February 2010 and August 2013. The aortic annulus sizing for prosthesis choice was done by TEE in 29 patients and by CT in 107 patients. Aortic calcium volume was measured in 67% of patients who have got CT. Follow-up was performed at 1, 6, 12 and 24 months post TAVI.

**Results:** Aortic annulus sizing by TTE and TEE echocardiography (TEE) were well correlated (r=0.73, p=0.0001, n=51) but were significantly lower than CT sizing (p<0.0001). The incidence of AR ≥2/4 was 13% and was not significantly different according to the strategy (echo vs. CT) of aortic annulus sizing for pros- theths from the Simvastatin and Ezetimibe in Aortic Stenosis (SEAS) study.

**Conclusion:** This study showed that aortic annulus sizing by echocardiography is significantly lower than sizing by CT. AR have an independent prognostic on survival. Prevention of aortic regurgitation is an important issue for the future of this technique.
P2374 | BEDSIDE
Dynamics of aortic annulus morphology during cardiac cycle: implication for TAVI procedure

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Purpose: The transcatheter aortic valve implantation (TAVI) is a technique in rapid expansion, the accurate measurement of the annulus size is the key point for the appropriate implantation of the valve prosthesis and for limit complications such as dislodgment, peri-valvular leakage, complete atrio-ventricular block, or annular rupture.

Aim of this study was the assessment of dynamics of aortic annulus morphology during cardiac cycle.

Methods: 14 patients (age 83, male/female 10/4) with severe aortic valve stenosis (TAVI group) and 10 patients (age 64, male/female 6/4) with suspected CAD (Control group) underwent coronary CT angiography (spiral ECG gated acquisition, Lightspeed VCT 128, GE Healthcare, iv administration of iodinated contrast medium. The image dataset (slice thickness 0.6 mm) was reconstructed at 10% increments over the cardiac cycle (phase 0 to 9 stating from tele-diastole), generating a 4-dimensional CT dataset. The following measurements of annulus were done for each ECG gated phase: maximum (MxD, mm), minimum (MnD, mm), mean diameter (MD, mm), ellipticity index (EI, (MxD/MnD)), cross-sectional area (CSA, mm²), and perimeter (Perim, mm).

Results: According the ECG-gated phase, the maximum, minimum and the percentage change of each parameter resulted the following in TAVI and Control group respectively: MxD: 27.95 ± 2.4 (phase 0), 35.0 (phase 5), 8.9% and 28.22 ± 3.5 (phase 0); 25.46 ± 3 (phase 5), 8.9% and 28.22 ± 3.5 (phase 0); 28.1 ± 2.5 (phase 5), 5.2%; MnD: 20.83 ± 2.4 (phase 1), 17.51 ± 2.4 (phase 6), 15.9% and 21.27 ± 2.6 (phase 2), 18.77 ± 2.6 (phase 6), 11.7%; MD: 23.7 ± 2.5 (phase 0), 21.7 ± 2.2 (phase 6), 8.4% and 24.4 ± 3.2 (phase 1), 12.1 ± 2.2 (phase 5), 9.8%; EI: 1.52 ± 0.2 (phase 6), 1.28 ± 0.1 (phase 2), 15.8% and 1.47 ± 2.1 (phase 6), 1.24 ± 0.1 (phase 2), 15.6%; CSA: 452.88 ± 102.7 (phase 0), 388.97 ± 84.1 (phase 6), 14.1% and 476.75 ± 131.6 (phase 0), 403.62 ± 73.3 (phase 6), 15.3%; Perim: 79.81 ± 9.0 (phase 0), 75.86 ± 11.1 (phase 5), 4.9% and 84.52 ± 13.8 (phase 0), 76.82 ± 9.1 (phase 7), 9.1%. We found no significant difference between TAVI and Controls.

Conclusion: The morphology of aortic annulus is modified throughout the cardiac cycle, the annulus resulted bigger in tele-diastole and smaller in systole and peri-diastole, the annulus shape resulted more elliptic in diastole than in systole. Perim showed the lesser percentage variation during cardiac cycle in TAVI patient.

P2375 | BEDSIDE
Morphology of the left ventricle tract assessed by tridimensional echocardiography and its impact in aortic stenosis severity evaluation

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The continuity equation quantification method of the aortic valve area (AVA) is dependent on laminar outflow tract (LVOT) diameter. It is assumed to be circular for the purpose of LVOT area calculation. This is one of the main sources of error of the method.

Purpose: Assess the LVOT morphology in patients with aortic stenosis (AS), comparing the dimensional changes of the LVOT with the calculated area of the LVOT when it is assumed circular and its influence in AS severity quantity.

Population and methods: 47 patients (pts), 33 males, age 74 ± 6.9 years with moderate or severe AS by transthoracic echocardiography (TTE) underwent transesophageal echocardiography (TOE). Tridimensional TOE acquisition of the LVOT and aortic valve in 3D zoom was performed. Planimetry of the aortic valve orifice and LVOT were performed after correct alignment of the cross sectional area in mesosystole with multiplanar reconstruction software.

The AVA for each patient was recalculated employing the LVOT area by 3D in the continuity equation (3DContEq). The morphology of the LVOT was classified according to the closest geometric shape.

Results: The LVOT was ellipse shaped in 40 pts, circular in 3 pts, other shapes 4 pts.

The area of the LVOT by 3D planimetry was significantly higher than when it was derived by the diameter in parasternal long axis LVOT = 3.12 ±0.63 cm², LVOT 3D = 3.79 ±0.80 cm², Mean difference = 0.67 ±0.63 cm² p <0.001. As a consequence the recalculated AVA by 3DContEq was bigger: AVA cont=0.89 ±0.25 cm², AVA calc=0.80 ±0.20 cm², mean difference =0.20 ±0.18 cm², p <0.001.

After correction of the LVOT area 12 pts considered severe by ETT were reclassified as moderate and 4 pts with moderate AS were reclassified as mild AS. 19 patients were classified as low gradient severe AS by ETT, of these 9 were considered moderate after correction of the LVOT area by 3D.

The correlation between the AVA by 3D planimetry was slightly better when the functional AVA was calculated with the continuity equation corrected for the LVOT 3D (r=0.74, p <0.001) than with the classic continuity equation (r=0.73, p <0.001).

Conclusion: The majority of these pts had ellipse shaped LVOT’s. The assumption of a circular LVOT in the continuity equation method overestimated the severity of stenosis. Calculating the AVA by the continuity equation with 3D planimetry of the LVOT increases the concordance with the anatomic area (3D planimetry) of the aortic valve and identifies pseudo-severe AS. The authors propose that the AVA calculation should be corrected with the LVOT 3D area if the AS seems significant by ETT.

P2376 | BEDSIDE
Area and perimeter derived effective annulus diameter: comparison with direct intraoperative sizing

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Objectives: A precise annulus sizing is of paramount importance for successful Transcatheter aortic valve implantation (TAVI). Currently, multislice computed tomography (MSCT) is the method of choice for determination of annulus dimensions. However, it remains unresolved whether 1) measurements should be performed in systole or diastole and 2) if calculation of the effective annulus diameter should be based on area or perimeter. Aim of our study was to compare MSCT results with direct intraoperative sizing of the annulus.

Methods: Conventional aortic valve replacement was performed in 52 patients, and the annulus was measured intraoperatively after decalcification using metric rulers. All patients had primarily been evaluated for TAVI including MSCT, but were deemed inappropriate for various reasons. The effective annulus diameter was determined derived by area (AsysA, AdiaA) and perimeter (AsysP, AdiaP) in systole and diastole, respectively. Furthermore, the potential change of prosthesis size was simulated for the various measurement approaches compared to IntraOp when TAVI would have been performed using the Edwards Sapien XT device.

Results: Best agreement with IntraOp was shown for AsysA by Bland-Altman analysis (mean difference [limits of agreement]): IntraOp vs. AsysA -0.36 mm [- 2.22 to 1.51]; IntraOp vs. AdiaA 0.42 mm [- 1.77 to 2.61]; IntraOp vs. AsysP -1.08 mm [-3.01 to 1.98] and IntraOp vs. AdiaP -0.45 mm [-2.81 to 2.61]. Simulation of TAVI showed less change of strategy with AsysA (26.9%), followed by AdiaA (30.0%), AdiaP (34.6%) and AsysP (38.5%).

P2377 | BEDSIDE
Impact of 3D aortic annulus shape and calcification on paravalvular regurgitation post TAVI

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Background: Aortic annulus is a 3D structure and has a major impact on paravalvular regurgitation. Method: Cardiac Computed Tomography was performed in 71 patients before TAVI. 3D Annulus shape was obtained point-by-point following the aortic cusps.

Area in mm²

<table>
<thead>
<tr>
<th>Shape</th>
<th>Area in mm²</th>
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<td>Diastole</td>
<td>32.4 mm²</td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>40.8 mm²</td>
<td></td>
</tr>
</tbody>
</table>

MSTN-annulus in systole and diastole.

Conclusion: Compared to surgical sizing area derived measurement in systostes represents the best approach for annulus determination. Perimeter derived measurement in systole may lead to overestimation of the annulus size.
insertion to aortic wall. In average 25 points covered the entire annulus circumference including the nadir and also the commissures of cusp insertion. Calcific 3D annular apposition was noted and compared with the echocardiography for detection of PAR after TAVI. We use a 12-quadrant clockwise segmentation. Annulus calcium surface (mm²) was measured and PAR was quantified using the planimetry of vena contracta.

**Results:** 71 patients were included in the study, 40 patients have mild or moderate PAR and 27 with moderate PAR. Annulus calcium was highly predictive of PAR (AUC 0.88) beyond valve calcium volume (AUC 0.7). In addition, annulus calcium (AC) location and site of PAR are closely related (Pearson’s correlation 0.84).

**Conclusion:** Annulus calcium 3D location strongly correlates with sites and number of paravalvular regurgitations. Annulus calcium protrusion accurately predicts PAR after TAVI.

**P2378 | BEDSIDE**

Echocardiography underestimates stroke volume and aortic valve area: implications for the classification of patients with small-area low-gradient aortic stenosis


**Purpose:** Discordance between small aortic valve area (AVA, <1.0 cm²) and low mean pressure gradient (MPG, <40 mmHg) affects a third of patients with moderate or severe aortic stenosis. We hypothesized that this is largely due to inaccurate echocardiographic measurements of the left ventricular outflow tract area (LVOTarea) and stroke volume alongside inconsistencies in recommended thresholds.

**Methods:** 133 patients with mild to severe aortic stenosis (AS) and 33 controls were enrolled. Participants underwent comprehensive echocardiographic and magnetic resonance imaging (MRI). Stroke volume and LVOTarea were calculated using both echocardiography and MRI, and the effects on AVA measurements assessed. The relationship between AVA and MPG measurements was then modeled with non-linear regression and consistent thresholds for these parameters calculated. Finally the impact of these modified AVA measurements and novel thresholds on the number of patients with small-area low-gradient AS was investigated.

**Results:** Compared to MRI, echocardiography underestimated LVOTarea (−0.5 [95%CI −2.4 to 1.3] cm²; Fig. A), stroke volume (−5.9 [95%CI −29.1 to 17.3] mL/m²; Fig. B) and thereby AVA (−0.22 [95%CI −1.11 to 0.67] cm²; Fig. C). An AVA of 1.0 cm² corresponded to MPG of 24 mmHg based on echocardiographic measures and 27 mmHg after correction with MRI-calculated stroke volumes. Based on conventional measures, 50 patients had discordant small-area low-gradient AS. Using MRI stroke volume and the revised thresholds, a 42% reduction in discordance was observed (n=29).

**Conclusions:** Echocardiography underestimates LVOTarea, stroke volume and therefore AVA. The thresholds based on current guidelines are inconsistent. In combination, these factors explain >40% of patients with discordant small-area low-gradient aortic stenosis.

**P2379 | BEDSIDE**

Prognostic value of stroke volume assessed using transthoracic 3d echocardiography in patients with aortic stenosis: a comparison with 2d echocardiography

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**Purpose:** Accurate assessment of disease severity is critical for the subsequent appropriate treatment in patients with aortic stenosis (AS). This study aimed to elucidate the prognostic value of stroke volume (SV) using 3D transthoracic echocardiography (TTE) in patients with AS.

**Methods:** This prospective study included 105 AS patients with aortic valve area (AVA) <1.0 cm² who underwent 2D and 3D TTE. SV was calculated according to the conventional Doppler and 3D methods. AVA was calculated using the continuity equation (CE). The definition of AS severity was based on indexed AVA (<0.6 cm²/m²). Major adverse cardiovascular events (MACE) were recorded in all patients.

**Results:** SV (64±15 vs. 55±21 ml) and AVA (0.70±0.21 vs. 0.60±0.22 cm²) were greater in the Doppler method than 3D method (all p<0.001). The prevalence of severe AS was lower in the Doppler method (72 patients, 69%) than 3D method (88 patients, 84%, p=0.003). During the mean of 184-day follow up, MACE were identified in 63 patients (60%), including 9 patients (8.6%) with cardiac death. In reclassification analysis, indexed AVA derived by 3D TTE improved the prediction of MACE by 10% (Fig. 1).

**Conclusion:** CE obtained from the conventional Doppler method has a potential risk for overestimation of SV and AVA in Japanese population. 3D SV have a stronger and additive prognostic value than the conventional Doppler method.

**P2380 | BEDSIDE**

Feasibility of assessing for preoperative left ventricular contractile function using two-dimensional speckle tracking echocardiography in patient with aortic stenosis


**Background:** The development of postoperative left ventricular dysfunction is a frequent complication in patients with severe aortic stenosis (AS) and implies a poor prognosis. The purpose of this study was to elucidate the predictive value of post-operative left ventricular dysfunction by using both tissue Doppler imaging and two-dimensional speckle tracking echocardiography (2D-STE) in patients with severe AS.

**Methods:** Forty patients with severe AS scheduled for aortic valve surgery were enrolled. The study population was divided into two groups, according to post-operative decrease in left ventricular ejection fraction (LVEF): Group 1 (G1), with postoperative LVEF decreases <10%, and Group 2 (G2), with postoperative LVEF decreases >10%. There were no significant difference in age between two groups (G1: 70±10 vs. 69±11 N=29, G2: 78±8 N=11). There were no significant differences in LVEF between two groups. Preoperative 2D-STE was carried out four chamber of longitudinal strain.

**Results:** Peak systolic velocity of mitral annulus (S) and global longitudinal strain (GLS) was significantly lower in G2 compared with G1 (S: p<0.03, GLS: p=0.003, Table). Especially, preoperative speckle tracking-derived longitudinal strain values at the level of the interventricular septum indicated a postoperative LVEF decreases of >10% (p=0.007, Table). Their indicative values were greater than other regional myocardium, but the most strong effective predictor was GLS.

**Conclusions:** GLS allows the accurate detection of early abnormalities in left ventricular contractile function. This tool might assist clinicians in the optimal timing of surgery in patients with severe AS.
The association between aortic valve weight and echocardiographic indices of aortic stenosis severity in 465 patients with isolated aortic stenosis and preserved left ventricular ejection fraction

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Purpose: To determine the relationship between aortic valve weight (AVW), as a measure of total AV calcium burden, and echocardiographic (echo) indices reflecting aortic stenosis (AS) severity in patients (pts) with normal ejection fraction (EF) undergoing aortic valve replacement (AVR) for severe isolated AS.

Methods: Between 2010-13, 465 patients (pts) undergoing AV replacement (AVR) for severe isolated AS (mean age 76.8 ± 9.3 yrs, 56% men, AV Index 0.36 (0.10 cm²/m²), EF=61.3±4.6%, 11% bicuspid valves), had AVs weighed (AVW=2.4±0.9 g), and preoperative echo studies. Pearson correlation was used to measure the linear association between AVW and the echo variables and a number of covariates were included through the calculation of partial correlation.

Results: Women have a lower AVW than men (2.1 (0.7) g vs. 2.6 (0.9) g, respectively, P<.0001) even when normalized for BSA (P=.01). Compared with pts with tricuspid valves or with low gradients, those pts with bicuspid valves or mean gradients ≥ 40 mmHg had higher AVW (P<0.0002 and P<.001, respectively). Other associations were similar between genders and pts with normal vs. low stroke volumes. The unadjusted and adjusted correlations of AVW with echo variables are shown in the table.

The correlations between AVW with AS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Corr coeff</th>
<th>p-value</th>
<th>Corr coeff</th>
<th>p-value*</th>
<th>Corr coeff</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensionless index</td>
<td>-0.27</td>
<td>&lt;.0001</td>
<td>-0.25</td>
<td>&lt;.0001</td>
<td>-0.25</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Mean gradient</td>
<td>0.21</td>
<td>&lt;.0001</td>
<td>0.21</td>
<td>&lt;.0001</td>
<td>0.16</td>
<td>0.0003</td>
</tr>
<tr>
<td>Peak gradient</td>
<td>0.21</td>
<td>&lt;.0001</td>
<td>0.20</td>
<td>&lt;.0001</td>
<td>0.18</td>
<td>0.0004</td>
</tr>
<tr>
<td>Peak velocity</td>
<td>0.20</td>
<td>&lt;.0001</td>
<td>0.20</td>
<td>&lt;.0001</td>
<td>0.18</td>
<td>0.0001</td>
</tr>
<tr>
<td>AV resistance</td>
<td>0.16</td>
<td>0.01</td>
<td>0.16</td>
<td>0.0001</td>
<td>0.17</td>
<td>0.0002</td>
</tr>
<tr>
<td>AV area</td>
<td>-0.04</td>
<td>0.05</td>
<td>-0.15</td>
<td>0.002</td>
<td>-0.16</td>
<td>0.003</td>
</tr>
<tr>
<td>Energy loss index</td>
<td>-0.11</td>
<td>0.04</td>
<td>-0.12</td>
<td>0.04</td>
<td>-0.15</td>
<td>0.02</td>
</tr>
<tr>
<td>LV stroke work loss</td>
<td>0.04</td>
<td>0.67</td>
<td>0.01</td>
<td>0.88</td>
<td>-0.02</td>
<td>0.81</td>
</tr>
</tbody>
</table>

*Adjusted for BSA; **adjusted for age, gender, BSA, diabetes, renal insufficiency, hypertension, CAD, heart failure, cardiac meds.

Conclusions: 1. In severe isolated AS with normal EF, AVW is most closely associated with dimensionless index. 2. Women have lower AVW than men even when adjusted for BSA, while bicuspid aortic valves have higher AVW than tricuspid valves. 3. These findings may help in the interpretation of non-invasive evaluation of AV calcium load and AS severity in challenging cases.

P2382 | BEDSIDE

Relationship between segmental longitudinal strain and symptomatic status in severe aortic stenosis: Real-time three-dimensional speckle-tracking echocardiography


Purpose: The aim of this study was to evaluate the relationship between strain by 3-dimensional (3D) speckle tracking echocardiography (STE) and symptomatic status in patients with severe aortic stenosis (AS) and normal left ventricular ejection fraction (LVEF>50%).

Methods: Conventional and 3D STE were performed in 69 patients (mean age 69.3 ± 14.8 yrs) with severe AS (aortic valve area < 1.5 cm², AV Vmax > 4 m/sec or mean PG > 40mmHg) and normal LVEF but without overt coronary artery disease. Severe AS patients were divided into two groups: asymptomatic (n=55) and symptomatic group (n=14).

Results: Global longitudinal strain (GLS) measured by 2D and 3D was not different in asymptomatic and symptomatic AS group. In 3D segmental LS analysis, basal LS was reduced in both. Interestingly, mid anterolateral and apical anterolateral 3D LS were significantly decreased in symptomatic AS group compared to asymptomatic (Fig. 1). 2D STE also showed the same results.

Figure 1. RT 3D LS in severe AS patients.

Conclusions: Three-dimensional segmental strain was related to symptomatic status in severe AS. Three-dimensional STE may give additional information in the decision-making process for patients with severe asymptomatic AS.
of cardiac function may be more sensitive than conventional cardiopulmonary exercise parameters in detecting early cardiac decompensation in patients with severe asymptomatic aortic stenosis.

### P2386 | BEDSIDE
Cardiopulmonary exercise testing in asymptomatic or equivocal symptomatic aortic stenosis

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**Objective:** To evaluate the feasibility, reproducibility and normal values of cardiopulmonary exercise testing (CPX), to assess the cardiac function from the measurements obtained, and to describe the information beyond that obtained from echocardiography and functional classification in patients judged asymptomatic or equivocal symptomatic from moderate to severe aortic stenosis (AS/ES-AS).

**Methods:** Prospectively, 131 patients (mean age 72±9.3 years and Vmax 3.92±0.77 m/s) with AS/ES-AS were evaluated by NYHA classification, echocardiography and CPX with inert gas rebreathing (IGR). The predicted normal values were set according to authoritative recommendations.

**Results:** CPX was feasible for 98% of the patients. On average, the patients reached 72±9.3% of the predicted peak oxygen consumption (pVO2) (reflects cardiac output) and 109±24% of the predicted pVO2/heart-rate (pO2pulse) (reflects stroke volume (SV)). A significant subnormal pVO2 (<83% of predicted) was noted in 26.1% of the patients. Abnormal trajectories for O2pulse and for O2pulse were found in 25.2% and 13.2% of the patients, respectively. The coefficient of variability by test-retest was 5.4% for pVO2 and 4.6% for pO2pulse. By IGR, the mean increase in SV from rest to exercise was 29±22%. A Vmax > 4 m/s was not associated with subnormal pVO2 or pO2pulse, lack of increase in SV, or higher frequency of abnormal trajectories. Kappa for NYHA class vs absolute and percentage reached of predicted pVO2 was low: 0.16 and 0.21, respectively. Increase in systolic blood pressure <20 mm Hg was not associated with abnormal pVO2, pO2pulse or trajectories.

**Conclusions:** CPX appears to be a promising tool for the diagnosis of functional limitation and hemodynamic compromise, serial assessments, and categorization of patients with AS/ES-AS.

### P2389 | BEDSIDE
Valvulo-arterial impedance is the best mortality predictor during long term follow-up in asymptomatic patients with moderate or severe aortic stenosis and normal ejection fraction

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**Introduction and aim:** Risk stratification is particularly complex in asymptomatic patients with hemodynamically significant aortic stenosis (AS). The aim of this study was to assess which hemodynamic/Doppler-echocardiographic parameter best predicts mortality, as a hardest clinical endpoint, in asymptomatic patients with moderate or severe AS and normal LV EF.

**Method:** This prospective study included 128 consecutive asymptomatic patients who met the criteria for a diagnosis of moderate or severe AS (aortic valve area (AVA) < 1.5 cm², mean gradient (Pmean) > 30 mmHg). The mean follow-up was 8 (1-24) years. Transthoracic echocardiography exam was performed according to European standard echocardiographic views. The mathematically derived parameters that represent LV workload and hemodynamic severity of AS, such as valvulo-arterial impedance (Zva), energy loss index (ELI) and stroke work loss (SWL) were calculated and compared during follow up. The Zva, ELI and SWL were calculated for all patients by direct patient examination or telephone interview. The ethics committee of the hospital approved the study, and all patients gave written informed consent.

**Results:** The mean age was 66.47±10.59 years. The mean AVA was 0.81±1.09 cm², mean pressure (Pmean) was 43.26±19.34 mmHg and Vmax was 4.27±0.44 m/s, while mean LV EF was 72.24±6.37%. Average values of NT-proBNP were high; 858.11±1710.62 pg/mL and mean E/E’ was 12.73±5.16. Mean Zva was 5.15±1.77 mg Hg m⁻¹ m², mean ELI was 0.59±0.20 cm² m⁻¹ m² and mean SWL was 39.24±11.67 W/m². During follow-up 61 patients (47.59%) underwent aortic valve replacement surgery. Out of 11 patients who died (8.59%), 10 died before being operated (one patient refused operation), while one patient died after surgery due to the postoperative infection. Based on Cox univariate analysis, the following were shown to be predictors of mortality: indexed stroke volume (SVI), Zva, A, S, ELI and aortic valve resistance (AVR). These parameters were further analyzed with Cox multivariate analysis and the Zva was found to be the best single predictor for mortality (HR: 1.734; CI = 1.397–2.152; p=0.001). The Zva value of 5.3 mmHg ml⁻¹ m² was identified as the best (cut-off) predictive value for the occurrence of death with sensitivity 67% and specificity 72%.

**Conclusion:** The Zva is the best mortality predictor in asymptomatic patients with moderate or severe AS and normal LV EF. However, future studies are needed to further focus on predictors of outcome in order to expand our knowledge on how to optimally select asymptomatic patients at risk who may benefit from early aortic valve replacement.

### P2387 | BEDSIDE
Clinical significance of serial BNP changes in asymptomatic patients with aortic stenosis

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**Background:** The ESC guidelines emphasized the usefulness of B-type natriuretic peptide (BNP) measurements for the management of asymptomatic patients with aortic stenosis (AS) and preserved left ventricular ejection fraction (LVEF). The aim of this study was to determine the impact on outcome of serial BNP changes during follow-up.

**Methods and results:** We studied 63 asymptomatic patients with AS (1.0±0.2 cm²) and preserved LVEF (69±6%) that underwent BNP level measurement at baseline and then after each 6- or 12-months. BNP significantly increased between baseline and the last measurement (101±140 vs. 160±229 pg/mL; p<0.001). Annualized BNP changes were calculated as the difference between the last and baseline BNP measurements divided by the time between them (24±16 months). Mean annualized BNP change was +47±10.53 pg/mL/year. After stratification for gender, there was a significant graded relationship between higher annualized BNP changes (according to tertiles) and decreased cardiac event-free survival (log rank test, p=0.017). Using Cox proportional hazards model, annualized BNP changes were significantly associated with increased risk of adverse cardiac events (HR: 3.03, 95% CI: 1.3–6.9; p=0.009).

**Conclusion:** In asymptomatic patients with AS and preserved LVEF, serial BNP changes may identify unmasked patients at higher risk of developing Class I indications for aortic valve replacement.

### P2388 | BEDSIDE
Risk prediction in aortic stenosis

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**Background:** Aortic stenosis (AS) is a progressive disease but there is incomplete understanding of the characteristics and outcomes associated with advancing age.

**Methods:** The Simvastatin and Ezetimibe in Aortic Stenosis population of 1,877 patients with mild/moderate AS was divided in two groups (younger/older) by the median age 67. Primary outcome was a composite endpoint of aortic valve replacement (AVR), congestive heart failure due to progression of AS (CHFAS) or death from cardiovascular causes.

**Results:** Mean age was 59.9 and 75.6 years in the younger and older group, respectively, followed for 4.3 years. The older group included more women (44.8 vs 32.7%), had more hypertension (58.9 vs 44.5%), prior atrial fibrillation (12.2 vs 6.9% p<0.01), higher total cholesterol (5.8 vs 5.7 mmol/L p=.031), smaller aortic valve area index (0.60 vs 0.65 cm²/m²), and used aspirin (2.5 vs 8.7%, both p<0.01) but similar left ventricular mass index (98 vs 97 g/m² p=.081) compared to the younger group. The younger group had been diagnosed with AS longer than the older group (3.0 vs. 2.5 years, p=0.002) and were more frequently
current or former smoker (58.9% vs. 51.6%, p < 0.002). 314 (32.7%) younger and 320 (35.1%) older patients reached the composite primary outcome (p=0.16), with no difference in AVR (p=0.20). CVD was more common among the older (HR 4.14, adjusted HR 3.02 CI 1.69-5.37, both p < 0.001). CHFAS was more common among older in unadjusted analyses (HR 3.40, p < 0.001), but not in adjusted analyses (p=0.11). CVD post- AVR was more common in the older group (HR 3.35 CI 1.40-8.02 p=0.007) but there was no difference in 30-day all-cause mortality post- AVR (p=0.11). CHFAS is an indication of surgical intervention, however only 11 (30.6%) of the older vs. 12 (100%) younger received AVR (HR 10.08 CI 4.01- 25.34 p < 0.001). All younger patients with CHFAS receiving AVR survived post- operative follow-up (1.5±1.3 year). The risk of CVD among older patients with CHFAS not receiving AVR was significantly higher compared to older patients receiving AVR (HR 8.61 CI 1.82-40.84 p < 0.02).

Conclusion: Older patients with AS have similar incidence of AVR and CHFAS but higher incidence of CVD. However, older patients with indication of AVR due to CHFAS do not receive AVR to the same extent as younger patients although older patients have similar 30-day post-operative mortality.

P2390 | BEDSIDE
Progression of aortic valve calcification in aortic stenosis - Impact of anatomy and severity. The COFRASA - GENERAC Study
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Background: Degree of aortic valve calcifications (AVC) is closely related to aortic stenosis (AS) hemodynamic severity but the influence of gender and valve anatomy has been seldom evaluated. In addition, the impact of baseline AS severity on AVC progression remained unclear.

Methods: In 295 patients with at least mild AS, we prospectively evaluated AS hemodynamic (mean pressure gradient, MPG) and anatomic severity (AVC score measured using tomography) at baseline and yearly thereafter.

Results: A good correlation was observed between AVC and MPG overall (r=0.70, p<0.0001) but for the same hemodynamic severity, AVC load was higher in patients with bicuspid than tricuspid aortic valve and in male than in female (p<0.008 and p=0.017 respectively). In multivariable analysis after adjustment for hemodynamic severity both gender (p<0.0001) and valve anatomy (p=0.001) were independent determinants of AVC load. Hemodynamic and anatomic changes were well correlated (r=0.55, p<0.0001) but AVC progression was strongly related to baseline severity (r=0.46; p<0.001).

Conclusion: older patients with AS have similar incidence of AVR and CHFAS but higher incidence of CVD. However, older patients with indication of AVR due to CHFAS do not receive AVR to the same extent as younger patients although older patients have similar 30-day post-operative mortality.

P2391 | BEDSIDE
Carotid intima-media thickness is a strong predictor of incident aortic stenosis: a prospective cohort study
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Purpose: Stenosis of the aortic valve is the most common valve disease requiring surgical valve replacement in western countries. Previous studies have suggested that aortic stenosis (AS) shares the same risk factor profile as coronary artery disease. To our knowledge no study has examined the relation of vascular ultrasound measurements with AS in a population-based study.

Methods: A random subset of middle-aged participants in the population-based Malmö Diet and Cancer study underwent ultrasound analysis of the right carotid artery, including measurement of intima-media thickness (IMT) in the common carotid artery (CCA) and the carotid bifurcation (BF). Subjects with prevalent AS were excluded, leaving 3522 participants for statistical analyses, of whom 50 had incident AS during up to 20 years of follow-up. Potential risk factors were tested for association with AS in age- and sex-adjusted and multivariable-adjusted Cox regression analyses. IMT-CCA and IMT-BF were analysed in separate models.

Results: Significant risk factors in age- and sex-adjusted analyses were (per 1 sd increase): high BMI, high LDL cholesterol, hypertension, diabetes, IMT-BF and IMT-CCA. In contrast, smoking, HDL, triglycerides, C-reactive protein, height, and leukocyte count were not associated with AS (p>0.05). In the multivariable-adjusted analysis, IMT-CCA and IMT-BF, LDL, and diabetes remained strongly and significantly associated with incident aortic stenosis (Table 1).

Conclusions: Traditional cardiovascular risk factors were individually associated with incident AS, but only IMT-CCA, IMT-BF, LDL, and diabetes remained independently associated in multivariable models. AS represents a vascular disorder strongly related to IMT, with implications for the pathophysiology and prevention of this disease.

Conclusions: Traditional cardiovascular risk factors were individually associated with incident AS, but only IMT-CCA, IMT-BF, LDL, and diabetes remained independently associated in multivariable models. AS represents a vascular disorder strongly related to IMT, with implications for the pathophysiology and prevention of this disease.

P2392 | BEDSIDE
The low-density lipoprotein-density-pressure theory identifies asymptomatic aortic stenosis patients benefiting from cholesterol-lowering therapy: the seas study
A. Greve1, C. Gohike-Baerwolf2, K. Boman3, K. Egstrup4, Y.A. Kesianemi5, S. Ray6, T. Pedersen7, P. Best8, N. Rajamannan9, K. Wachtell9, 1 Rigshospitalet - Copenhagen University Hospital, Cardiology B2142, Copenhagen, Denmark; 2 University Heart Center Freiburg-Bad Krozingen, Bad Krozingen, Germany; 3 Umea University, Umea, Sweden; 4 Odense University Hospital, Odense, Denmark; 5 Oulu University Hospital, Oulu, Finland; 6 Manchester Academic Health Sciences Centre, Manchester, United Kingdom; 7 Oslo University Hospital, Oslo, Norway; 8 Mayo Clinic, Rochester, United States of America; 9 Glostrup Hospital, Glostrup, Denmark

Purpose: Examine if the low-density lipoprotein (LDL)-density-pressure theory identifies aortic stenosis (AS) patients that benefit from cholesterol-lowering therapy.

Methods: Asymptomatic patients with mild-to-moderate AS randomized (1:1) to 40 mg Simvastatin + 10 mg Ezetimibe combination vs. placebo and ≥2 in-study echocardiograms. Primary endpoint in this substudy was impact of randomization on the association between LDL changes and progression in AS severity, as determined by peak aortic jet velocity. Treatment effect was analyzed by separating patients in 4 groups according to LDL levels (≥160 mg/dl and AS severity (≥3.0 m/sec).

Results: 1,682 patients followed for a mean of 4.4 years (7,373 patient-years of follow-up). Among those with elevated LDL and mild AS at baseline, LDL lowering was associated with less AS progression in the active-arm (p=0.18 [95% CI: 0.13 - 0.24], p=0.001), but not in those receiving placebo ([0.0 – 0.98 [95% CI: 0.19 to 0.03], p=0.14). For LDL levels (≥160 mg/dl and AS severity in the 3 other groups (all p>0.42 for interaction). Similarly, the treatment effect was also
Table 1. Achieved cholesterol-lowering impeded aortic stenosis progression in patients with mild aortic stenosis and elevated low-density-lipoprotein levels (p=0.0003).

<table>
<thead>
<tr>
<th>LDL levels (&lt;160 mg/dL)</th>
<th>p*</th>
<th>LDL levels (&gt;160 mg/dL)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velocity (&gt;3.0 m/sec)</td>
<td>0.05</td>
<td>Active (n=60): 0.001, p=0.76</td>
<td></td>
</tr>
<tr>
<td>Placebo (n=51): 0.02, p=0.71</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Velocity (&lt;3.0 m/sec)</td>
<td>0.42</td>
<td>Active (n=49): 0.18, p=0.003</td>
<td></td>
</tr>
<tr>
<td>Placebo (n=45): 0.08, p=0.14</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: LDL—low-density lipoprotein; Active treatment: 40 mg Simvastatin + 10 mg Ezetimibe. *p-value for interaction (difference in slope) by randomization status.

Impact of low flow state on cumulative mortality of high-risk patients undergoing transcatheter aortic valve intervention


Purpose: Although low ejection fraction (LVEF) has been reported to be an independent risk factor of increased mortality following surgical aortic valve replacement, its impact on post-procedural transcatheter aortic valve intervention (TAVI) outcome has yielded conflicting results. Moreover, a low flow state, i.e. reduced left ventricular stroke volume index (SVi), can occur with both reduced and preserved LVEF. The objective of this study was to evaluate the impact of pre-procedural SVi, LVEF, and transvalvular gradient on 2-year all-cause mortality following TAVI.

Methods: Patients with severe and symptomatic aortic stenosis (AS) (effective orifice area [EOA]<1.0cm²) who underwent TAVI at our institution were prospectively enrolled. Primary end-point was 2-year all cause mortality was defined according to the criteria proposed by the Valve Academic Research Consortium.

Results: We included 116 patients (mean age: 80.1±7.3 years). Sixty-nine (59%) patients had normal flow (SVi>35ml/m²) and 47 (40.5%) low flow (SVi<35ml/m²). Overall, the primary end point occurred in 20 (17%) patients during a median follow-up period of 24 months. Patients with low flow had higher 2-year all cause mortality compared with those in the normal flow group (31.8% versus 16.0%, p=0.01). Mortality was also increased in patients with low LVEF compared with those with normal LVEF (31.8% versus 16.0%, p=0.01). Patients with low mean gradient (<40 mm Hg) had higher 2-year all cause mortality compared with those in the normal flow group (28.0% versus 15.0%, p=0.01). By multivariate analysis SVi was the only independent predictor of 2-year mortality (p=0.01). LVEF was not associated with detectable difference in AS progression (cumulative mean difference 0.01 m/sec [95% CI: -0.1 to 0.1, p=0.80]).

Conclusions: Low SVi but not low LVEF or low gradient is an independent predictor of 2-year cumulative mortality following TAVI in high risk patients with severe AS. SVi should be integrated in the risk stratification process of these patients.

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Transcatheter aortic valve implantation in patients with low gradient aortic stenosis and preserved left ventricular ejection fraction

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Background: Transcatheter Aortic Valve Implantation (TAVI) is an established alternative to surgery for selected patients with severe symptomatic aortic stenosis. Low-gradient aortic valve stenosis (LAGAS) with preserved LV ejection fraction (AHA 1.0cm², MAVG <40mmHg and LVEF >50%) is thought to be due to low stroke volume and patients are said to have a poorer prognosis. The impact of TAVI in these patients has not been previously explored.

Methods: All patients undergoing TAVI with CoreValve at our institution were eligible for study inclusion. Detailed quantitative echocardiography was performed according to ASE guidelines. Only patients with LVEF >50% at baseline were included and further stratified according to baseline mean aortic valve gradient (<10mmHg or >40mmHg). Echocardiographic and clinical outcomes were compared at 12 months.

Results: 38 patients (mean age 83±8 years, 46% female, mean EuroScore 17±5%) were analysed, 12 month echo and clinical data was available for 34 patients (55±8 years, 49% female, mean EuroScore 16±6%). Mean gradient (29.6±0.4% vs. 40mmHg (4 patients were lost to follow up [1 LGAS]). There were no deaths in either group. At 12 months, echo parameters were similar for both groups, including LVEF, global longitudinal strain and markers of diastolic function. Quality of life score (Minnesota Living with Heart Failure Questionnaire) and functional status (NYHA class) post TAVI were similar in both groups.

Conclusion: TAVI is an effective therapy for patients with low gradient severe aortic stenosis with similar improvements in post procedural aortic valve haemodynamics, quality of life and functional status as those patients with high gradient severe aortic stenosis.

P2399 | BEDSIDE

Patients with low-flow, low-gradient aortic stenosis are in substantial risk after Transcatheter Aortic Valve Implantation, but survivors demonstrate a substantial clinical improvement

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Purpose: Previous studies showed that patients with impaired left ventricular (LV) function and low-flow, low-gradient (LFLG) aortic stenosis (AS) are associated with high operative risk and poor long-term outcome after surgical aortic valve replacement. The aim of this study was to investigate the clinical outcome of LFLG AS after transcatheter aortic valve implantation (TAVI).

Methods: 580 consecutive patients in high operative risk underwent TAVI with the Medtronic Coregessor Edwards Sapien prostheses at our institution between June 2008 and October 2012. Full data of 469 patients was collected. Of these, 258 patients presented with normal-flow, high gradient (NFHG) AS (aortic surface area (ASA) >1.0 cm², mean gradient (0.3mmHg) -30 mmHg, LVEF 1.0 cm², 36 patients with LFLG AS (<1.0 cm², 0.3mmHg LVEF <30%). Clinical follow-up, echocardiography and measurements of NT-pro-BNP levels were analyzed at 10 days, 4 weeks, 6 months, 1 year and 1 year after TAVI.

Results: Patients with LFLG AS had a much lower survival rate at 12 month after TAVI compared to patients with NFHG AS (41% vs. 86%, p<0.0001). Nevertheless, surviving patients with LFLG AS showed a significant and steady rise in LVEF in TAVI after 4 weeks (before 24.2±4.7% vs. 30 days 37.0±13.2%, p<0.05), after 6 month (39.5±12.1%) and 1 year (52.0±4.3%) and a reduction of NT-proBNP (before 11653±8085 ng/L vs. 12 month 1844±1273 ng/L, p<0.05). Furthermore, these patients showed reduced symptoms of heart failure resulting in an improved NYHA functional class (LFLG AS vs. NFHG: 4± weeks: -1.2±0.7 vs. -1.3±0.6, p<0.05; 16 months: -1.3±0.4 vs. -1.2±0.7, p=0.12; 52 months: -1.6±0.4 vs. -1.2±0.8, p=0.6).

Conclusions: This study shows that the all-cause mortality, 12 month after TAVI in patients with LFLG AS is notably high. However, surviving patients presented an enormous improvement in myocardial function and a high clinical benefit.

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Paradoxical low gradient aortic stenosis is not an end-stage of disease as it progresses to high gradient aortic stenosis: an echocardiographic follow-up study


Background: Paradoxical low gradient severe aortic stenosis (PLG-SAS) is a recently described subset of aortic stenosis which is, since its description, highly challenging. Some authors consider this new pattern as a more advanced stage of disease than high gradient severe aortic stenosis (HG-SAS) whereas others think just the opposite. The aim of the present work was to test this theory by studying the progression of their mean gradient over time.

Methods: Between 2000 and 2010, 105 consecutive patients (51 men, 77.9± years) with PLG-SAS (mean transvalvular gradient <40 mmHg, indexed aortic valve area <0.6cm²/m² and left ventricular ejection fraction ≥50%) at the time of inclusion had an echocardiographic follow-up ≥6 months. Mean gradient progression was assessed in a first time by using a paired t-test and in a second time, using a Kaplan-Meier analysis where the recording of a high gradient (>40 mmHg) was considered as an event.

Results: During a median follow-up of patients (range 6–68 months), the severity of aortic stenosis had progressed significantly: the mean gradient increased from 29.6±6 mmHg to 38.1±11 mmHg (p<0.001). At the end of follow-up, 46 (45%) had reached the stage of HG-SAS, 38 (37%) remained at the stage of
PLG-SAS but significantly increased their mean transvalvular gradient (from 26±5 mmHg to 32±5 mmHg, p<0.001) and 18 either had maintained or decreased their mean transvalvular gradient over time. Interestingly, in 11 out of these 18 patients, the reduction in mean transvalvular gradients was contemporary to the development of left ventricular dysfunction.

Conclusion: PLG-SAS progresses almost systematically to the classical HG-SAS. This suggests that PLG-SAS represents a less advanced stage of disease than HG-SAS.

P2399 | BEDSIDE

Outcomes of patients with moderate-severe and severe aortic stenosis and preserved left ventricular ejection fraction: impact of stroke volume index

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Background: We sought to determine predictors of outcomes in a contemporary group of moderate-severe & severe aortic stenosis (AS) patients & preserved ejection fraction, based on stroke volume index (SVI) & AS subtypes.

Methods: We studied 1637 AS patients with aortic valve area (AVA) ≤ 1.3 cm² evaluated between 1/07-12/08 (excluding severe other valve disease). Clinical & echo data was recorded. Patients were classified into following AS subtypes: moderate-severe (n=368, AVA 1.1-1.3 cm², 68±15 years, 62% men), standard severe (n=670, AVA ≤ 1 cm² & mean gradient ≥ 40 mm Hg, 70±12 years, 60% men & paradoxic severe (n=591, AVA ≤ 1 cm² & mean gradient ≥ 40 mm Hg, 71±12 years, 56% men). SVI was calculated as: [left ventricular outflow tract (LVOT) velocity time integral x LVOT area]/body surface area. SVI ≤35 ml/m² was normal. All-cause mortality was recorded.

Results: At 4.7±1.2 years, 1024 (63%) had AV replacement (AVR) & 359 (22%) patients died. 64% had normal SVI. Mortality was different in moderate-severe (19%), standard severe (20%) paradoxic AS (26%) (log-rank p<0.01). Mortality was different in normal vs. abnormal SVI (20% vs. 26%, log-rank p<0.01). On multivariable time-dependent survival analysis, age (Hazard ratio or HR 1.04 [1.03-1.05]), functional class or FC (HR 1.44[1.28-1.62]), lower glomerular filtration rate ≥ 60 mL/min/1.73 m² (HR 0.79 [0.64-0.97]) & AVR (HR 0.32 [0.25-0.41]) impacted survival (all p<0.0001), while AVR predicted improved survival.

Conclusion: In patients with moderate-severe & severe aortic stenosis & preserved low flow, low gradient aortic stenosis.

P2400 | BEDSIDE

Natural history of paradoxical low-flow low-gradient aortic stenosis

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Background: Among patients (pts) with severe aortic stenosis (sAS) and preserved ejection fraction (EF), those with low flow (LF) and low gradient (LG) have an adverse prognosis. It has been proposed that this condition represents a late-stage point of sAS. We investigated if LFLG sAS is the evolution of a normal-flow (NF) high-gradient (HG) stage or a different entity directly progressed from moderate aortic stenosis.

Methods: From the transthoracic echocardiography (TTE) database, we identified pts with sAS (aortic valve area <1 cm²) and preserved EF (>50%), and from these pts with LFLG sAS, defined as stroke volume index <35 ml/m² and mean aortic valve gradient <40 mm Hg, who had at least one additional TTE within 5 years prior to the index qualifying TTE. These pts were age/sex/date matched 2:1 (follow-up) were analyzed, based on transvalvular pressure gradient (hazard ratio =0.97, 95% CI: 0.95-0.99; p=0.01).

Conclusion: Low SVI measured invasively is frequent in patients with severe AS and preserved LV EF and is a powerful and independent predictor of survival. SVI should be systematically measured and used as an additional parameter for risk stratification of patients with severe AS.

P2399 | BEDSIDE

Impact of low flow on long-term survival in patients with severe aortic stenosis and preserved left ventricular ejection fraction: a cardiac catheterization study

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Background: We studied 1637 AS patients with aortic valve area (AVA) ≤ 1.3 cm² evaluated between 1/07-12/08 (excluding severe other valve disease). Clinical & echo data was recorded. Patients were classified into following AS subtypes: moderate-severe (n=368, AVA 1.1-1.3 cm², 68±15 years, 62% men), standard severe (n=670, AVA ≤ 1 cm² & mean gradient ≥ 40 mm Hg, 70±12 years, 60% men & paradoxic severe (n=591, AVA ≤ 1 cm² & mean gradient ≥ 40 mm Hg, 71±12 years, 56% men). SVI was calculated as: [left ventricular outflow tract (LVOT) velocity time integral x LVOT area]/body surface area. SVI ≤35 ml/m² was normal. All-cause mortality was recorded.

Results: At 4.7±1.2 years, 1024 (63%) had AV replacement (AVR) & 359 (22%) patients died. 64% had normal SVI. Mortality was different in moderate-severe (19%), standard severe (20%) paradoxic AS (26%) (log-rank p<0.01). Mortality was different in normal vs. abnormal SVI (20% vs. 26%, log-rank p<0.01). On multivariable time-dependent survival analysis, age (Hazard ratio or HR 1.04 [1.03-1.05]), functional class or FC (HR 1.44[1.28-1.62]), lower glomerular filtration rate ≥ 60 mL/min/1.73 m² (HR 0.79 [0.64-0.97]) & AVR (HR 0.32 [0.25-0.41]) impacted survival (all p<0.0001), while AVR predicted improved survival.

Conclusion: In patients with paradoxic severe AS & abnormal SVI have higher mortality compared to other subtypes. Greater mortality is predicted by increasing age, low GFR and higher FC, while AVR predicted improved survival.

P2399 | BEDSIDE

Impact of low flow on long-term survival in patients with severe aortic stenosis and preserved left ventricular ejection fraction: a cardiac catheterization study

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Background: Previous studies suggested that a low flow defined as an indexed stroke volume (SVI) ≤35 ml/m² may be an important determinant of outcome in patients with severe aortic stenosis (AS). However, its quantification using echocardiography may be subject to error measurement. The aim of this study is to determine the impact of low SVI determined during cardiac catheterization on long-term survival among patients with severe aortic stenosis and preserved LV ejection fraction.

Methods and results: Between 2000 and 2010, 768 patients with preserved LV EF (>50%) and severe AS (valve area <1cm²) without other valvular or other heart disease underwent cardiac catheterization. SVI was derived from catheterization data.

Mean age was 74±8 years, 42% were female, 46% had coronary artery disease and mean LVEF was 72±10%. Overall, low SVI was found in 27% of AS patients. As compared to patients with normal SVI, those with decreased SVI were significantly older (p<0.0001) and had more frequently atrial fibrillation (p=0.0001); in addition, they had lower LVEF (p=0.04), aortic valve area (p<0.0001), mean pressure gradient (p<0.001), systemic arterial compliance (p<0.0001) and higher systemic vascular and pulmonary resistances (p<0.0001).

Conclusion: In patients with severe aortic stenosis and preserved LV EF and with normal LVEF, low stroke volume was associated with worse long-term survival. It seems that low flow is an easy, important and independent predictor of poor outcome in patients with severe AS.
Ten-year survival was significantly reduced in patients with higher Zva (50 remains associated with reduced survival as compared to low Zva, in patients survival (hazard ratio [HR]=1.12 95% CI: 1.009-1.22; p=0.03). Of interest, high Zva as compared to those with lower Zva (67 erful and independent predictor of survival. Zva should be used as an additional to be predictive for the development of a LG/AS (Global Strainase study). After a median follow-up of 13 months, there were 29 aortic valve re- placements (AVR) and 30 deaths. In a multivariate Cox proportional hazards model, presence of RVD (HR=3.36, p=0.006) was an independent predictor of all-cause mortality, despite adjustment for AVR (p=0.007) and presence of con- tractile reserve (p=0.36) (Panel A). Patients with RVD who underwent AVR had worse survival and similar to those patients who did not undergo AVR (Panel B). Baseline RVD added incremental value in the risk stratification of these patients (X2 increased from 10.7 to 16.6, p=0.005).

P2402 | BEDSIDE

Prognostic impact of global left ventricular hemodynamic afterload in severe aortic stenosis with preserved ejection fraction: a cardiac catheterization-based study

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Background: Previous studies suggested that global left ventricular (LV) hemo- dynamics afterload as assessed by valvulo-arterial impedance (Zva), may be an independent predictor of mortality in patients with severe aortic stenosis (AS) and preserved LV ejection fraction (LVEF). However, its quantification using echocar- diography may be subject to error measurement. The aim of this study is to de- termine the prevalence and impact on long-term survival of high Zva, purposely measured by cardiac catheterization.

Methods and results: Between 2000 and 2010, 768 patients with preserved LVEF (>50%) and severe AS (valve area <1cm²) without other valvular heart disease underwent cardiac catheterization. Zva was derived from catheteriza- tion data and calculated using following formula: mean aortic gradient × systolic blood pressure / indexed LV stroke volume. Zva was considered high when >5 mmHg/mL/m² based on previous studies. Mean age was 74±8 years, 88% were females, 46% had coronary artery disease and mean LVEF was 72±10%. Overall, high Zva was found in 42% of all AS patients. Patients with high Zva were significantly older (p<0.0001), and more often fe- male (p<0.0001), they had significantly smaller aortic valve area (p<0.0001), higher indexed LV stroke volume (p<0.0001), and significantly lower cardiac output (p<0.0001) and systemic arterial compliance (p=0.006), reduced systolic arterial compliance (p<0.0001), but higher systemic vascular resistances (p<0.0001).

Ten-year survival was significantly reduced in patients with higher Zva (50%±5%) as compared to those with lower Zva (67%±3%; p<0.01). After adjustment for all other risk factors, Zva was independently associated with reduced long-term sur- vival (hazard ratio [HR]=1.95; 95% CI: 1.099-1.22; p<0.03). Of interest, high Zva remains associated with reduced survival as compared to low Zva, in patients with normal LV stroke volume, but was no longer significant in low flow patients (LV stroke volume<60 mL: 49±8vs. 69±4%; p=0.012; LV stroke volume<60mL: 49±7 vs. 53±13%; p=0.96).

In a large cardiac catheterization-based study, high Zva, esti- mated invasively, is frequent in patients with severe AS, and appears as a power- ful and independent predictor of survival. Zva should be used as an additional parameter for risk stratification of severe AS, more particularly in patients with normal flow.

P2402 | BEDSIDE

Right ventricular dysfunction and prognosis in patients with low-flow, low-gradient severe aortic stenosis


Background: Patients with low LVEF, low-flow low-gradient severe aortic stenosis (LFLG AS) represent a challenging cohort with high morbidity and mortality. Al- though right ventricular dysfunction (RVD) is an important predictor of outcomes after CABG, its impact on the risk-stratification of patients with LFLG AS is un- known.

Methods: 65 consecutive LFLG severe AS patients (80% men) who underwent low-dose dobutamine stress echocardiogram between May/04 and June/13 were studied. The mean age was 74±9 yrs; LVEF 29±10%; LV area index 0.49±0.1 cm²/m²; mean AV gradient 22±7 mmHg. Contractile reserve defined as ≥20% increase in stroke volume was present in 40% of patients. RVD defined as tricus- pid annular plane systolic excursion <16 mm, measured in the apical 4-chamber view, was present in 37 patients (57%).

Results: After a median follow-up of 13 months, there were 29 aortic valve re- placements (AVR) and 30 deaths. In a multivariate Cox proportional hazards model, presence of RVD (HR=3.36, p=0.006) was an independent predictor of all-cause mortality, despite adjustment for AVR (p=0.007) and presence of con- tractile reserve (p=0.36) (Panel A). Patients with RVD who underwent AVR had worse survival and similar to those patients who did not undergo AVR (Panel B). Baseline RVD added incremental value in the risk stratification of these patients (X2 increased from 10.7 to 16.6, p=0.005).

MORE ON TAVI

P2405 | BEDSIDE

Pre-existing aortic regurgitation protects against the adverse effects of paravalvular leakage after transcatheter aortic valve implantation

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Purpose: Paravalvular leakage (PVL) after transcatheter aortic valve implantation (TAVI) is associated with mortality. Hypothetically, a hypertrophied and stiff left ventricle does not well tolerate acute aortic PVL, versus one preconditioned by pre-existing aortic regurgitation (AR). Accordingly, we evaluated the effect of pre- existent AR.

Methods: We included all consecutive patients who underwent a TAVI in our centre from June 2009 to July 2013. We prospectively evaluated the severity of pre-existent AR and PVL by echocardiography. Mortality was registered at 12 and 24 months.

Results: In total, 399 patients (mean age 80±9.6 years, 44.9% male) under- went a TAVI. Moderate/severe pre-existent AR existed in 56 patients (14.0%) and moderate/severe PVL occurred in 50 patients (12.5%). The 1-year survival rate was lower in patients with a PVL versus no PVL (71.0% vs. 81.1%; p=0.019).

In those who developed a PVL, pre-existent AR independently predicted 1- and 2-year survival (HR: 2.8, 95%CI: 1.6 to 5.2; p=0.001, resp. HR: 2.3, 95%CI: 1.3 to 4.2; p=0.002). Pre-existent AR did not influence survival in patients who devel- oped no PVL.

Conclusions: Pre-existent AR independently predicts long-term survival, espe- cially in patients with residual PVL. Thus, pre-existent AR is a protective factor to tolerate acute PVL after TAVI.
**P2406 | BEDSIDE**

**Predictors and long-term prognosis of paravalvular regurgitation after transcatheter aortic valve implantation**

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**Introduction:** Paravalvular regurgitation (PVR) after transcatheter aortic valve implantation (TAVI) has been associated with increased morbidity and mortality. Our aim was to study TAVI PVR occurrence and to determine its long-term impact on outcomes.

**Methods:** Single centre prospective registry of 145 consecutive TAVI procedures in 144 patients (pts) with aortic valve stenosis. Mean age was 80±7.7 years, 69 (41%) male, 65 (58.6%) treated with self-expandable and 69 (41.4%) with balloon expandable valve. Mean aortic annular diameters were 22.±2.7mm (coronal) and 20.8±2.1mm (sagittal), by angioTC. The protocol first transphenoidal echocardiography (TTE) was performed in-hospital and assessed PVR according to color Doppler fraction of prosthetic ring circumference. The second TTE evaluation was realized at a median of 11 IQ [4-25] months.

Logistic regression was applied to determine the independent predictors of PVR at first TTE among clinical, imaging and procedural variables. The event rate of death, rehospitalization, NYHA III/IV and VARC2-eficacy endpoint was estimated by binary logistic regression for the presence and severity of PVR. Survival curves for the presence and severity of leak were constructed (log rank test).

**Results:** PVR was identified in 96 pts (66%) in the first TTE, it was mild, moderate and severe in 56%, 8.6% and 1.4% respectively. 2 pts loss their mild leaks and eight developed PVR during the follow up. Univariate predictors for PVR were: chronic renal failure, peripheral arterial disease, previous thoracic radiation, thoracic malformations, porcelain aorta, transfemoral vascular access, previous aortic valvulotomy, type of implanted prosthetic valve and the absence of balloon dilation after implantation (p<0.01). At multivariate analysis, only auto-expandable prosthesis implantation remained a predictor of PVR (OR 3.94, 95% CI [1.88 to 8.33], p=0.0001).

During the follow-up (15.6 months [5.9-26.9]) 25 deaths (17.2%) and 35 efficacy events (95% CI [1.88 to 8.33], p=0.0001).

**Conclusions:** In our study, PVR occurred in 96% of pts (66%) in the first TTE, it was mild, moderate and severe in 56%, 8.6% and 1.4% respectively. Survival analysis evidenced a non-significant split of the curves according to the presence and severity of PVR (mild vs. moderate/severe: p=0.142). The prevalence of paravalvular regurgitation after TAVI is considerable and it appears to be associated with the type of implanted prosthetic valve. It remains stable during the follow-up and does not have an impact in clinical outcomes.

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**P2407 | BEDSIDE**

**Influence of baseline ejection fraction on prognostic value of paravalvular aortic regurgitation in patients after transcatheter aortic valve implantation**

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**Background:** Moderate/severe paravalvular aortic regurgitation (P AR>2) after transcatheter aortic valve implantation (TAVI) has been associated with increased mortality. Whether baseline ejection fraction (EF) has influence on prognostic value of P AR is unclear.

**Methods:** Between January 2007 and December 2012, 434 patients with native severe aortic stenosis underwent TAVI in our hospital. Patients were divided in two groups as preserved EF group (EF ≥40%, n=362) and low EF group (EF <40%, n=72). P AR before discharge was assessed by transthoracic echocardiography and impact of PAR on mortality were compared in the two groups.

**Results:** At baseline, low EF group had lower age and aortic gradients and worse renal function as compare to preserved EF group. In addition, low EF group had higher prevalence of diabetes, coronary artery disease and significant baseline mitral and aortic regurgitation. In-hospital mortality was significantly higher in low EF group as compared to preserved EF group (11.0% vs 2.5%, p <0.01). After TAVI, PAR>2 occurred 23% of the patients and was significantly associated with reduced 2-year survival rate only in the low EF group (82% vs 35%, log-rank p <0.001 and 89% vs 89%, log-rank p=0.2 in preserved EF group). In multivariate analysis, PAR>2 had 2.9-fold increase in mortality risk in low EF group, whereas in preserved EF group, PAR>2 was not associated with a significant mortality risk.

**Conclusions:** In our study, PAR>2 after TAVI was associated with increased 2-years mortality only in patients with low baseline EF. Our data suggest that baseline EF is a potential modifier on prognostic value of PAR. Careful attention to PAR is needed especially for low baseline EF patients.

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**P2408 | BEDSIDE**

**Paravalvular regurgitation after TAVI, a comparison**

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**Background:** Significant paravalvular aortic regurgitation (PVAR) after transcatheter aortic valve implantation (TAVI) impacts long-term mortality. The Direct Flow Medical (DFM) aortic valve has a repositionable non-metallic pressurized support structure designed to minimize aortic regurgitation.

**Objectives:** Prospective non-randomized comparison of PVAR after DFM versus SAPIEN XT valve implantation in high risk patients with severe aortic stenosis.

**Methods:** One hundred thirty nine consecutive high surgical risk patients (mean age 82.±6.4y, 47% male, mean log EuroScore 18.6%) with severe aortic stenosis were evaluated immediately post implant for PVAR by transesophageal echo (TEE). PVAR was graded as “none or trace”, “mild”, “moderate”, “severe” according to the VARC criteria. One hundred eight patients received a SAPIEN XT and 31 patients a DFM valve. Both groups did not differ in patients demographics, log EuroScore, severity of baseline aortic stenosis, degree of valve calcification based on CT, and valve sizing, which was performed by TEE and CT.

**Results:** Thirty day mortality 2.8% for SAPIEN XT and 0% for DFM. For PVAR see Table.

**Conclusions:** Compared to SAPIEN XT the DFM valve significantly reduces PVAR which may have an impact on long-term prognosis.

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**P2409 | BEDSIDE**

**Identification of parameters contributing to the variability of the aortic regurgitation index in a two-center TAVI cohort**

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**Background:** For precise quantification of paravalvular aortic regurgitation (AR) in patients undergoing transcatheter aortic valve implantation (TAVI), the assessment of hemodynamics with the AR Index is helpful. In this study, we assess parameters, which impact the AR Index.

**Methods:** Pre- and post-procedural Indices was calculated as ratio of the transvalvular gradient between diastolic blood pressure (DBP) in the aorta and left-ventricular end-diastolic pressure (LVEDP) to the systolic blood pressure (SBP): [(DBP-LVEDP)/SBP] x 100. Multivariate regression analysis was used to identify parameters, which contribute to the variability of the AR Index.

**Results:** 523 patients (age 81.±6.5 years) underwent TAVI in two independent institutions. The post-procedural AR Index was significantly associated with 2-year mortality (P<0.001). In multivariate regression analysis, the AR Index was independently associated with STS score (P<0.020), EF (P<0.049), cover index (P<0.001), heart rate (P<0.027), and the pre-procedural AR Index (P<0.001) but not with the prosthesis type (P=0.77).
In patients with an AR index ≥25 after TAVI, outcome was independent from the pre-procedural AR Index. However, patients with an AR Index <25 could be further stratified by the pre-procedural AR Index (Figure): while patients with low pre-procedural AR Index had an only 2.2-fold higher risk (P = 0.006), a pre-procedural high AR Index ≥34 was associated with a 4.5-fold higher 2-year mortality risk (P < 0.001).

Conclusions: Patients with an AR Index below 25 have a significantly impaired prognosis after TAVI. In these patients, a low pre-procedural AR Index before the procedure is associated with a more favorable outcome and might indicate resilience against the impact of paravalvular aortic regurgitation.

P2411 | BEDSIDE
Hemodynamic evaluation of aortic regurgitation after transcatheter aortic valve implantation using cardiac magnetic resonance imaging: a comparative study with echocardiography and angiography
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Background: More-than-mild periprosthesis aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) has been associated with increased mortality and morbidity. The AR index (ARI) has been recently proposed as an objective indicator for the severity of AR after TAVI as compared to c-MRI. Furthermore, there is no correlation between c-MRI and TTE or angiography. Further studies are mandatory to confirm our results in a larger population.

Methods: 118 patients (pts.) treated with transforamal TAVI between 10/08 and 10/13 and examined with cardiac MRI 1-2 weeks after TAVI were included in this analysis. The dimensionless AR index was calculated from post-TAVI pressure tracings according to the formula: ([diastolic blood pressure - left ventricular end-diastolic pressure]/systolic blood pressure) * 100. Phase-contrast MRI was conducted to quantify the degree of AR. A regurgitant fraction (RF) <15% was graded as mild, 16-30% as moderate, 31-50% as moderate-severe and >50% as severe. A RF <1% was classified as no AR.

Results: A mean age of the cohort was 81 years (range 52-92 y); 70 pts. (59%) were women. 68 pts. (58%) were treated with the CoreValve prosthesis and 50 pts. (42%) received a Sapien XT valve. The mean AR calculated at the end of the TAVI procedure was 26.7±6.3. Cardiac MRI revealed a median RF of 4.8% (range 0.03-47.6%). 16pts. (14%) had a RF <1% and were classified as no AR, 80 pts. (68%) had mild AR, and 22 pts. (18%) had significant AR (15 pts. with moderate and 7 with moderate-severe AR). No significant correlation was observed between the calculated AR index and the DPTI-Index-adj (r = 0.30; p = 0.06). In contrast, there was a good correlation between TTE and angiography (r = 0.6; p < 0.001). TTE underestimated AR by one degree in 9 patients, and by two degrees in 6 patients as compared to c-MRI.

Conclusions: The results of our study suggest that TTE and angiography may underestimate the severity of AR after TAVI as compared to c-MRI. Furthermore, there is no correlation between c-MRI and TTE or angiography. Further studies are mandatory to confirm our results in a larger population.

P2413 | BEDSIDE
Diagnostic and prognostic value of NT-proBNP in patients with paravalvular leakage after transfemoral aortic valve implantation
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Background: N-terminal segment of B-type natriuretic peptide pro-hormone (NT-proBNP) provides prognostic information in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation (TAVI). Furthermore, NT-proBNP is associated with higher mortality risk in patients with aortic regurgitation. The aim of the present study was to examine the prognostic and diagnostic potential of NT-proBNP as a biomarker in patients with paravalvular aortic regurgitation (AR) after TAVI within a 12-month follow-up period.

Methods: A total of 395 consecutive patients with severe aortic stenosis undergoing elective TAVI were included in the study. AR was measured on the second day after TAVI using echocardiography. Blood samples were collected before TAVI and 4 h and 1, 2, 3, and 6 days afterwards. Serum was processed immediately and frozen at -80°C until assay. NT-proBNP was measured in serum with an electrochemiluminescence immunoassay using monoclonal antibodies. Patient follow-up was for 1 year.

Results: Paravalvular AR > II° was observed in 196 (49.7%) patients, and in 46 (11.7%) patients the AR was ≥ II° (16.9%) patients died during the one-year follow-up. Patients with AR post-TAVI had a higher mortality rate (41 [20%] vs. 2% for stable AR) (P <0.05) compared with those without AR. There were no differences in baseline characteristics between deceased and surviving patients. NT-proBNP levels were similar at baseline between survivors and non-survivors (AUC = 1 ≥ 2.540.0 ng/L [996.7-511.8] vs. AUC = 1 ≥ 2.127.0 ng/L [1.045.0-4.972.5].
respectively: P=0.6), whereas NT-proBNP levels on the second day after TAVI were higher in non-survivors with AR > 1° compared with survivors, where AR < 1° (6,881.0 ng/L [3,103.0-10,279.0] vs. 2,758.0 ng/L [1,346.0-4,419.0]; P=0.001). The risk of mortality was higher if NT-proBNP was increased by at least 10% between the first and second day after TAVI (multivariate Cox regression analysis adjusted for age, estimated glomerular filtration rate, left ventricular ejection fraction, and atrial fibrillation: hazard ratio 2.6; P=0.03). The second day after TAVI was the best time point for predicting one-year mortality (AUC 0.807 [95% CI 0.83-0.9; P=0.004]).

Conclusion: NT-proBNP provides prognostic information predicting mortality within 1 year in patients with AR after TAVI. These findings demonstrate that serial NT-proBNP measurements can be used for risk stratification and determination of further therapeutic measures in patients with AR after TAVI.

P2414 | SPOTLIGHT
Transcatheter valve in valve is an elegant solution to a surgical problem

Background: Reoperation for degenerated bioprosthesis is a surgical challenge with long-term risk of osteoporosis and mortality compared to the primary operation. The introduction of transcatheter heart valve (THV) therapy has opened a new treatment option for these patients. Valve-in-valve offers a big advantage: You see the valve frame on x-ray and therefore easily can adjust your x-ray to the new situation, and secondly to that avoid using contrast. However, it is very important to have exactly knowledge of the type and size of the inoperated bioprosthesis, to be able to choose the right THV size and also at which height in the bioprosthesis the optimal implantation for the THV is.

Methods: Since the start of our THV programme with the Edwards Sapien valve system September 2008 we have treated 19 patients with degenerated bioprosthesis. All patients were discussed for conventional surgery and recommended for THV therapy. We have rejected one patient because the inoperated valve (Mitrflow 21mm) was too small for available transcatheter valves.

Results: We have treated 13 patients with degenerated aortic bioprosthesis, 5 with degenerated mitral bioprosthesis and 1 with degenerated tricuspid bioprosthesis, see tables for baseline data, procedural data and follow-up data. Periprocedurally, one patient died of circulatory failure and one suffered a stroke (fortunately good recovery). One valve embolized to the left ventricle because of operator failure (missed to retract the so-called pusher), the patient was operated immediately with good result. All surviving patients have good valve function and almost no paravalvular leakage. We have seen no late complications.

Conclusion: Valve-in-valve implantation offers a new treatment option for patients with degenerated bioprosthesis. On one hand the procedure is straightforward forward because you clearly see the inoperated bioprosthesis, on the other hand it is mandatory to know the exact type and size of the bioprosthesis to avoid miszising and misplacement.

ATRIAL FIBRILLATION: MISCELLANEOUS

P2416 | BEDSIDE
The French screening campaign of atrial fibrillation in general practice: qualitative evaluation of the campaign (awareness, interest, and impact on daily practice)
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Context: Atrial fibrillation (AF) affects nearly 750,000 patients in France and this number is expected to double by 2050. AF is a severe disease with important consequences in terms of morbidity and mortality but still under-diagnosed. An AF screening campaign (Profil FA) in 16 French sites with a simple questionnaire based on heartbeat measurement, AF linked symptoms and thromboembolic patient risk (CHADS-VASC score) was deployed in 2013 among family physicians (GP).

Results: 365 questionnaires were collected (response rate of 60%) and analyzed. Overall, 76% GP estimated the campaign has positively raised their awareness (min 48.5% in Bourgogne and max 100% in Côte d’Azur/Nice). The campaign helped to point out the relative high frequency of AF in elderly patients (65% GP) and to systematically measure heartbeat in this population (81% GP). Cardiologist orientation was higher in GP with higher AF awareness. Overall the campaign helped better collaboration with cardiologist for 58% participating GP. Cardiologist orientation was well accepted by 85% patients but with better level of acceptance in rural environment (P=0.047).

Conclusion: The simple Profil FA campaign aiming to detect unknown AF in patients > 65y helped to raise GPs’ awareness of the disease in GP, improved collaboration with cardiologist. The satisfaction index shows the positive impact of this campaign for the GPs. Nevertheless attention should be paid to interregional differences to optimize outcomes of campaign.
AF incidence by familial association.

**Conclusions:** Familial AF was associated with an increased incidence of AF in first-degree relatives compared with the general Danish population. Our results suggest that familial AF is a major risk factor for developing this prevalent and morbidity-prone cardiac arrhythmia.

**P2419 | BEDSIDE**

High physical fitness; associated with increased or reduced atrial fibrillation risk in middle-aged men?

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**Purpose:** Smaller studies have demonstrated increased atrial fibrillation (AF) risk among long-endurance trained athletes. However, limited and inconsistent data are available concerning level of fitness and AF risk in the general population. We aimed to investigate associations between measured physical fitness and incident AF in men.

**Methods:** In 1972-1975, as part of a prospective cardiovascular survey, 1997 healthy middle-aged Norwegian men were tested with a symptom-limited bicycle exercise ECG test. Physical fitness was calculated as total exercise work capacity divided by body weight. Incident AF was documented by scrutiny of medical records in all Norwegian hospitals. Risk estimations were analysed in quartiles of age-adjusted PF using adjusted Cox proportional hazards models.

**Results:** During 35 years of follow-up, 253 men developed AF (13%). Men with age-adjusted physical fitness in the upper quartile had significantly reduced long-term AF risk in multivariate analyses compared with the rest of the cohort. Further analyses in deciles and subgroups with baseline elevated blood pressure, showed that the men with the very highest fitness had slightly increased risk compared to those with high (but not extreme) fitness.

**Table 1. Risk of AF in hazard ratios according to quartiles of age-adjusted physical fitness**

<table>
<thead>
<tr>
<th>Age-adjusted physical fitness</th>
<th>Hazard ratio*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>the remaining quartiles (n=1487)</td>
<td>65 (12.7%)</td>
<td>188 (12.6%)</td>
</tr>
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</table>

**Conclusions:** High physical fitness in healthy middle-aged men was associated with approximately 25% lower long-term risk of incident AF. Men with very high fitness, however, seemed to have a slightly increased risk compared to those with more moderate high fitness, especially if their resting blood pressure was elevated.

**P2420 | BEDSIDE**

Galectin-3 is associated with worse clinical outcome in patients with atrial fibrillation: A substudy from the ARISTOTLE trial

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**Methods:** The ARISTOTLE trial included patients with AF and increased risk of stroke who were randomized to aspirin 5 mg b.i.d. or warfarin (INR 2-3). Levels of Galectin-3 were measured, by the Abbott assay, in plasma samples obtained at randomization from 1998 patients. The association between baseline levels of Galectin-3 and the composite outcome of stroke, systemic embolism (SE) or death, and major bleedings was evaluated in Cox proportional hazard models.

**Results:** Quantities of Galectin-3 were Q1=13.7, Q2=13.8-16.4, Q3=16.5-20.2, and Q4=20.3-25.7 pmol/L. The median level of 17.7 mg/mL, Increasing CHA2DS2-VASC and HAS-BLED scores were associated with higher level of Galectin-3. During follow-up (median 3.0 years), 261 stroke/SE/deaths and 125 major bleedings occurred. Annual rates of stroke/SE/deaths ranged from 2.62% in Q1 to 7.63% in Q4 and the hazard ratio (95% CI) for Q4 vs Q1 was 2.94 (2.02-4.27) (effect of biomarker p<0.0001). Annual rates of major bleedings ranged from 1.69% in Q1 to 3.66% in Q4 and the hazard ratio for Q4 vs Q1 was 2.19 (1.30-3.69) (p=0.0236).

**Conclusions:** In patients with AF, Galectin-3 was associated with increased risk of stroke, SE or death, and major bleeding. Our findings suggest that this novel biomarker might help refine risk stratification in AF patients.

**P2421 | BEDSIDE**

Familial occurrence and resolution of left atrial thrombus during dabigatran therapy: a JHRS survey report

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Since dabigatran (Dabi) was launched on March 14, 2011 in Japan, electrical cardioversion (EC) of atrial fibrillation (AF) has been planned and attempted during dabigatran therapy, providing an opportunity to examine both formation and resolution of atrial thrombus (AT) in this clinical setting. Accordingly, the Japanese Heart Rhythm Society made a retrospective survey of the incidence and the fate of AT among 299 institutions from December 2011 to January 2013. There were a total of 199 patients (pts) with planned EC who also underwent either transesophageal echocardiography (TEE) or computed tomography to rule out AT before EC. Of these 199, AT was found in 9 pts (4.5%). These 9 pts with AT were younger (68.7 vs 61. 3 years, p<0.075) and had higher CHADS2 scores (2.1 vs 0.9, p=0.037) than those without AT. Of the 9 pts with AT, 1 developed AT within 3 weeks of Dabi 150mg bid, whereas the remaining 8 pts received a lower dosage, 110mg bid, for 4 weeks or longer. Notably, in 3 of these 8, the AT was found before the second TEE was done - 6wks later, disclosing a complete resolution of AT in 5, i.e., on the same dosage in 2, after an increased dosage of Dabi in 2, and after switching to warfarin in 1. EC was carried out in both 190 pts without AT and 5 with AT after its resolution. There were 2 cases of stroke developing 3 and 21 days, respectively, after EC while on Dabi. Importantly, no AT was found before the third TEE in those cases. The men had CHADS2 score >0, but received inappropriately low dosage of 110mg bid. There was 1 case of major bleeding in the large intestine during Dabi therapy. In conclusion, AT developed in 4.5% of AF pts receiving Dabi. Older pts with higher CHADS2 score receiving inappropriately lower dosage or shorter duration of Dabi administration are likely to have AT, which can resolve with a prolonged or increased dosage. Nevertheless, AT can also develop even under a recommended dosage and duration of Dabi. Therefore, it is important not only to pay attention to Dabi dosage and duration before and after EC, but to perform TEE before EC in all Dabi pts.

**P2422 | BEDSIDE**

Rhythm control strategies in atrial fibrillation: inter-country differences in Europe. Follow-up data from the PREFER in AF registry

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**Purpose:** Rhythm control can be a valid strategy for patients with paroxysmal or persistent atrial fibrillation (AF) based on factors such as the degree of symptoms, age or activity levels. This strategy needs to be frequently supplemented by the use of antiarrhythmic drugs or interventions. There is a lack of comparative data concerning the use of these resources in different parts of Europe.

**Methods:** The PREFER in AF registry – European Registry in Atrial Fibrillation (PREFER in AF) prospectively enrolled unselected patients with AF in 7 European countries including France (FR), Germany (GE), Italy (IT), Spain (SP) and the United Kingdom (UK) from Jan 2012 to Jan 2013 in 461 centres. Here we report the patterns of rhythm control strategies used at baseline and within 1 year of follow-up (FU).

**Results:** At baseline, in 7243 patients enrolled, 30.0% had paroxysmal, 24.0% had persistent and 26.5% had permanent atrial fibrillation. Half of them received rhythm control therapy. During the 1 year of FU 5% of patients underwent pharmacological cardioversion (from 2.4% in GE to 7.8% in IT). Electrical cardioversion was performed in 7.6% of patients. Electrical cardioversion was one of the preferred methods in the UK for a rhythm control strategy (14.5%) and it was performed mainly in an outpatient setting (82.6%). On the other hand, a T wave during cardioversion were absent. In 6 cases, the men had CHADS2 score ≥0, and received inappropriately low dosage of 110mg bid. There was 1 case of major bleeding in the large intestine during Dabi therapy. In conclusion, AT developed in 4.5% of AF pts receiving Dabi. Older pts with higher CHADS2 score receiving inappropriately lower dosage or shorter duration of Dabi administration are likely to have AT, which can resolve with a prolonged or increased dosage. Nevertheless, AT can also develop even under a recommended dosage and duration of Dabi. Therefore, it is important not only to pay attention to Dabi dosage and duration before and after EC, but to perform TEE before EC in all Dabi pts.
tion procedures during FU was reduced (from 18.1 to 7.6% and from 5.0 to 3.3%, respectively), possibly reflecting unsuccessful attempts to restore sinus rhythm. Among antiarrhythmic drugs amiodarone remained as the most frequently used in 16.8% of patients (from 8.8% in UK to 25.2% in FR). Flecaïnide or propafenone was used in 9.6% (from 3.7% in UK to 14.3 in FR), and sotalol in 4.0% (from 1.1% in SP to 6.6% in FR). The use of dronedarone was significantly lower during FU (2.1%; from 0.2% in FR to 4.9% in GE) as compared with baseline (4%).

Conclusions: Despite a relative homogeneity in the percentage of patients receiving rhythm control therapies for AF in these different European countries, there are big regional variations regarding the preferred method between interventional (ablation/electrical cardioversion) or pharmacological strategies.

P2423 | BEDSIDE

Atrial fibrillation (AF) occurs in ~30% of patients undergoing coronary artery bypass grafting (CABG) and in 40% of patients after valve surgery, von Willebrand factor (vWF) is a biomarker of endothelial dysfunction and prothrombotic state. vWF is an independent risk factor for adverse events in AF patients. We included consecutive haemodynamically stable patients undergoing programmed cardiac surgery with cardiopulmonary bypass pump. We determined vWF before cardiac surgery and recorded AF development by prolonged ECG monitoring. We evaluated fibrosis in tissue sample form the right atrial appendage. We studied 100 patients for CABG (n=56) or aortic valve replacement. 29 patients developed post-surgical AF. We found higher levels of plasma vWF in CABG patients versus valvular patients (200±66 vs 157±84 I Ud/l; p=0.015). We found an association between vWF levels and interstitial fibrosis (OR 1.01 95% CI (1.00-1.03), p=0.042) and perivascular fibrosis (OR 1.01 95% CI (1.00-1.02), p=0.017) in the tissue (Fig 1). An association of the patient type with AF development was shown (p=0.034). Thus, we decided to investigate the prognosis in the two cohorts separately. We observed that vWF values above the 4th quartile were predictive of AF at a borderline significance [OR 4.5 95% CI (0.98-20.6), p=0.053]. In a multivariate model adjusted by clinical and demographic data (p<0.15 in univariate analysis) vWF levels remained as independent prognostic predictor for AF in ischaemic patients [OR 6.3 95% CI (1.14-34.71), p=0.035]. Valvular patient showed no association between vWF and AF development.

P2424 | BEDSIDE

Predicators for new-onset post-operative atrial fibrillation in patients undergoing aortic valve replacement

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Aim: 1. Defining the independent predictors for new-onset post-operative atrial fibrillation (POAF) in patients (pts) undergoing aortic valve replacement (AVR) and their adjusted value for calculation of a predictive risk score. 2. Assessment of the independent prognostic value of the LV diastolic dysfunction and left atrium (LA) dilatation for POAF development in these pts. 3. Identifying the predictors for recurrent atrial fibrillation (AF) and their implications for postoperative course in AVR pts.

Material and method: Prospective study on 802 pts who underwent AVR for atrial stenosis (456pts) or aortic regurgitation (AR) (346pts). Patients were evaluated clinically and by echocardiography (including TDI) preoperatively and postoperatively at 10, 20 and 30 days. All were in sinus rhythm without history of AF. Statistical analysis used SYSTAT and SPSS programs for regression analysis and for relative risks and correlation coefficient calculations. Multivariable analyses were adjusted for age and gender including left ventricular ejection fraction (LVEF)<35%, restrictive LV diastolic filling pattern (LVDFP), renal insufficiency and logistic EuroSCORE (p<0.20).

Results: POAF occurred in 320 of 862 patients (39.9%). 1. Regression analysis identified as independent predictors for POAF: restrictive LVDFP (RR=23.42), preoperative AR (RR=10.31), LA dimension in dex >30mm2 (RR=13.92), advanced age (RR for 10-year increase=2.09), LVEF<35%, LV enddiastolic volume (LVEDV)=55mm, higher body mass index, NYHA class III/IV, comorbidities 2. The presence of a restrictive LVDFP increased the POAF risk by 23.42 fold and the rate of POAF increased exponentially with diastolic dysfunction severity (p<0.001).

Conclusions: 1. The independent predictors for POAF initiation after AVR were: restrictive LVDFP, preoperative AR, advanced age, LVEDV >55mm, LVEF ≤35%, obesity, NYHA class III/IV and comorbidities 2. Restricted LVDFP and LA dilatation has a powerful independent and incrementally predisposing value for the initiation of POAF after AVR and their evaluation may be very useful during risk stratification of patients undergoing cardiac surgery. 3. The only independent predictors for recurrent POAF after AVR were: restrictive LVDFP, older age, LA dimension index ≤45mm<sup>2</sup>/m<sup>2</sup>, LVESEV <85cm<sup>2</sup>, bivacal venous cannulation, moderate mitral regurgitation (MR), severe pulmonary hypertension (PHT).

P2425 | BEDSIDE

Efficacy of omega-3 fatty acids alone or in combination with antioxidant vitamins on postoperative atrial fibrillation prevention: a meta-analysis

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Purpose: The effect of omega-3 polyunsaturated fatty acids (PUFA) on the prevention of postoperative atrial fibrillation (POAF) remains controversial based on individual studies. The aim of this meta-analysis was to ascertain the protective role of PUFA on POAF when it was used alone or in combination with antioxidant vitamins.

Methods: Studies were identified through PubMed, CENTRAL, EMBASE, and review reference lists of relevant papers. The odds ratio (OR) was calculated for POAF. Statistical analyses were performed with Review Manager 5.0.

Results: 11 randomized controlled trials with 3137 patients were included in the analysis. 9 studies reported isolated administration of PUFA as the sole intervention, 3 administered concomitant vitamins C and E therapy. Combined result showed that the use of PUFA alone did not reduce the incidence of POAF compared with the control (OR: 0.76; 95% confidence interval [CI]: 0.57-1.03; P=0.08; I²=52%). However, combination therapy with PUFA and vitamins C and E reduced the incidence of POAF by 68% (OR: 0.32; 95% CI: 0.17-0.60; P=0.0005; I²=28%).

Conclusions: Combination therapy with PUFA and vitamins C and E is effective in the prevention of POAF while PUFA alone not.

P2426 | BEDSIDE

Cardioversion of atrial fibrillation or atrial flutter decisively improves severity and type of sleep disordered breathing

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Purpose: Sleep disordered breathing (SDB) with obstructive sleep apnea (OSA) is associated with an increased risk of onset or recurrence of atrial fibrillation and atrial flutter. We sought to prospectively document SDB frequencies, type and severity in patients with atrial arrhythmias and we aspired to determine whether cardioversion into sinus rhythm has an immediate influence on type and severity of SDB.

Methods: A consecutive group of 138 patients (67±10.3 years, 67.4% male) was prospectively enrolled in our study and underwent multichannel cardiorespiratory polygraphy (PG) screening before and immediately (within 24 hours) after electrical cardioversion into sinus rhythm. In addition PG studies were repeated after four weeks of CV.

Results: 95.2% of the study population patients with atrial fibrillation (n=119; 119±18 days after CV); n=51 (40.18%) had SDB with an Apnea-Hypopnea Index (AHI) of ≥5/h. Immediately after CV AHI decreased significantly (23.4±16.3/h to 16.3±11.5/h, p<0.001). In contrast, after four weeks of follow up overall SDB severity was comparable to prior CV, even if atrial dysrhythmia did not recur for four weeks follow up. However, central respiratory events markedly improved with a reduction of patient’s presenting with central sleep apnea directly after CV: n=53 (42.7%) to n=23 (26.7%), p<0.001. In addition, there was a trend towards a further reduction in central events after 4 weeks of follow-up (n=8, 20%, p<0.3).

Conclusions: SDB is highly prevalent co-morbidity in patients with atrial dysrhythmia. While CV seems to have no long lasting effect on total AHI, this study reveals a significant reduction in central respiratory events. This may be explained by unmasking preexisting obstructive respiratory events. These findings may impact on diagnostic PG and postoperative cardioversion performed after restoration of cardiac rhythm. Thus, the optimal time span between CV and diagnostic PG leading to therapeutic indications need to be determined by further studies.
**P2427 | BEDSIDE**
Pharmacokinetics and pharmacodynamics of dabigatran etexilate 75 mg BID in patients with severe chronic kidney disease: prospective validation of a post hoc determined dose

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**Purpose:** Dabigatran etexilate (dabigatran) is a direct oral thrombin inhibitor approved for prevention of ischemic stroke in patients with non-valvular atrial fibrillation. Dabigatran is predominantly renally excreted (<30%) and is not metabolized significantly. The goal of the present study was to evaluate the pharmacokinetics of dabigatran etexilate (PK) and pharmacodynamics (PD) of this dose in patients with severe CKD.

**Methods:** In this open-label study, 15 patients received dabigatran 75mg BID for 7 days (steady state) followed by 4 days of wash-out. PK and PD blood samples were collected every 24 hours and full profiles over the dosing interval were obtained on the first and last day of dabigatran intake.

**Results:** Based on interim data from 10 patients (CrCl 15-29ml/min), the geometric mean (geometric coefficient of variation) Cmax.ss and AUClauss of total dabigatran etexilate were 0.59ng/ml (61.8%) and 2380ng·h/ml (59.8%), respectively. No drug accumulation occurred at the end of the treatment period. The observed mean concentration of dabigatran correlated well with values predicted by the PK model (Fig. 1).

**Figure 1.** Observed and predicted concentration-time profiles of total dabigatran after administration of dabigatran etexilate 75mg BID.

No patient developed an adverse cardiovascular event or major bleed. Final data in 15 patients will be presented at the congress.

**Conclusion:** The results confirm that, on average, the dabigatran etexilate 75mg BID regimen achieves the targeted drug exposure in patients with severe CKD without accumulation.

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**CATHETER ABLATION OF ATRIAL FIBRILLATION**

**P2429 | BEDSIDE**
First application of a novel, multi-site, high-resolution epicardial, mapping approach

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**Purpose:** Ablative therapy of atrial fibrillation (AF) is aimed at targeting either the trigger or substrate perpetuating AF. At present, there are no diagnostic tools for identification of the arrhythmogenic substrate. The goal of the present study was to assess the feasibility and safety of a novel, multi-site high-resolution epicardial mapping approach.

**Methods:** 150 consecutive patients underwent intra-operative, high-resolution epicardial mapping of the entire atria (using 60-128 unipolar electrodes/1-4 cm²) during sinus rhythm (SR) and acutely induced or persistent AF. Activation, voltage and conduction maps were created automatically at every location. Haemodynamic parameters, mean arterial pressure (MAP), right atrial pressure (RA), ST-segment alterations (ST) and level of anaesthesia (bispectral index (B.I.S)) before and during SR/AF mapping were compared.

**Results:** SR and AF was present in respectively 120 and 30 patients; AF was non-inducible in 10. Average AF duration was 5.3±6.7 minutes per patient needing 3±3 AF inductions in order to complete AF mapping. The total mapping time was significantly reduced by introduction of a larger mapping electrode (4 cm²), respectively 25±5 versus 15±5 minutes (p<0.0001). Hemodynamic parameters before and during SR mapping were respectively MAP 70±11/69±11 mmHg (p<0.22), RA 10±4/10±4 mmHg (p<0.15), ST 0.09±0.04/-0.08±0.49 mm (p<0.31) and BIS 37±9/39±6 (p<0.06). During AF, these values were MAP 71±11 vs 67±10 mmHg (p<0.004) and RA 10±4 vs 11±4 mmHg (p<0.0001). B.I.S did not differ between AF and SR (p=0.91). In the entire study population, a total of 11,675 seconds were obtained from 2235 atrial sites. Stability of the mapping electrode was demonstrated by a beat-to-beat variation of SR cycle length and peak-to-peak amplitude of the unipolar electrogram recorded from the central area of the right atrial appendage, respectively less than 0.04±14.42 ms and -0.01±0.53 mV. Complications were not observed.

**Conclusion:** Intra-operative multi-site, high resolution epicardial mapping of the atria is feasible and safe.

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**P2430 | BEDSIDE**
Validation of the coronary vessels near the ablation line on the mitral isthmus in the chronic phase after the catheter ablation

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**Purpose:** The linear catheter ablation on the lateral mitral isthmus (LMI) often requires radiofrequency (RF) energy delivery inside the coronary sinus (CS) or the great cardiac vein (GCV) which runs close to the left circumflex coronary artery (LCX). The acute occlusion of the LCX close to the ablation site in the cardiac venous system can be associated with a higher risk of acute occlusion of the coronary artery. The aim of the present study was to evaluate the influence of linear ablation at the LMI on the anatomy of LCX, CS and GCV by cardiac multi-detector computed tomography (MDCT) in the chronic phase, i.e., 1 year after ablation.

**Methods and results:** We performed MDCT on 28 patients (22 males, age 59.4±10.7 years) both before and after linear ablation on the LMI. The LMI ablation was performed under the guidance of the CARTO system with 3D geometric reconstruction of the left atrium (LA) from MDCT images. RF energy was delivered with 20–35 W with a saline irrigation speed of 17 or 30 ml/min. The mean lesion depth in the LCX artery (LCX) was 78.6±16.7 mm (59.6±18.4 mm, respectively). No drug accumulation occurred at the end of the treatment period. The observed mean concentration of dabigatran correlated well with values predicted by the PK model (Fig. 1).

**Figure 1.** Observed and predicted concentration-time profiles of total dabigatran after administration of dabigatran etexilate 75mg BID.

No patient developed an adverse cardiovascular event or major bleed. Final data in 15 patients will be presented at the congress.

**Conclusion:** The results confirm that, on average, the dabigatran etexilate 75mg BID regimen achieves the targeted drug exposure in patients with severe CKD without accumulation.

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**P2431 | BEDSIDE**
MRI characterization of cryoballoon and radiofrequency ablation lesions after pulmonary vein isolation

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**Introduction:** Cryoballoon (CA) and radiofrequency (RF) ablation are effective techniques to treat patients with paroxysmal atrial fibrillation (AF). Cryo-enhanced cardiac magnetic resonance (DE-CMR) allows the identification of ablation lesions (scar) and gaps. We aimed to compare the DE-CMR characteristics of the ablation lesions and gaps between both CA and RF ablation in patients with paroxysmal AF, and evaluate the clinical implications (recurrence rate).

**Methods:** We prospectively included 33 patients with paroxysmal AF undergoing a first procedure (9 RF, 14 CA). A DE-CMR was performed 6±3 months postablation. The endocardium and epicardium of the left atrium (LA) were manually segmented on axial plane slices. A 3D volume-rendered LA reconstruction was created using the segmented DE-CMR data. A pixel signal intensity map was projected on the 3D reconstruction and color-coded to display healthy areas and scar. The gap size was defined as the proportion (%) between the gap length and the total perimeter of the PV antrum. To evaluate the gap location, each group of ipsilateral PVs was divided into 4 quadrants (anterior, posterior, carina and superior or inferior).

**Results:** We analyzed a total of 92 PVs (36 RF, 56 CA). There were gaps in 80.6% and 91.1% of PVs in RF and CA group, respectively. The gap size was 31%±14% in the RF and CA group, respectively (p=0.217). The mean location of the gaps differed between groups: the inferior quadrant of the right inferior PV in the RF group (78% vs. 86% in CA group, p=0.624) and the superior quadrant of the left superior PV in the CA group (93% vs. 44% in the RF group, p<0.01). After 8 (6-12) months follow-up, 33% and 64% in the RF and CA group had recurrences, respectively (p=0.214).

**Conclusion:** Anatomic gaps on DE-CMR were common after RF and CA ablation. There was a trend toward a higher recurrence rate in the CA group compared to RF group; this finding might be related to a bigger gap size in the CA group or the differences in the location of the gaps between techniques.
Catheter ablation of atrial fibrillation

P2431 | BEDSIDE
Cryoballoon to esophagus distance predicts low esophageal temperatures during pulmonary vein isolation using the second generation cryoballoon
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Purpose: Catheter ablation of atrial fibrillation (AF) using the second generation cryoballoon (CB2) has been associated with low luminal esophageal temperatures (LET) and <20% esophageal lesions if NO LET cut off value has been applied. We sought to determine predictors of low LET analyzing anatomical and procedural data.

Methods: Patients (pts) undergoing a 28mm CB2-pulmonary vein isolation (PVI) procedure were included. An esophageal temperature probe (TP) was introduced and served as LET monitor. CB freeze duration was set to 240s and premature CB freeze termination was led by LET < 15°C to avoid LET 12°C. A video recording system recorded simultaneously 28mm CB and esophagus temperatures. The shortest fluoroscopic distance between the CB and the LET probe was always measured (LAO 40°, RAO 30°) and correlated with LET. Low esophageal temperature was arbitrarily defined as LET < 25°C. All patients underwent an esophageal endoscopy 24 hours after the procedure.

Results: 161 CB applications in 23 pts (16 male, 20 paroxysmal AF, 65±12 years) were recorded and analyzed. The initial LA inferior PV was characterized by the lowest LET but warmest CB temperature. 26/161 (16%) applications were characterized by a short anatomical and fluoroscopic distance between the PV anatomic subset and the esophagus, and greatest CB temperatures. A significant linear correlation between CB-Probe distance and LET could be demonstrated (Pearson r=-0.49, p<0.0001). Post PVI esophageal endoscopy revealed just one lesion in a single patient (1/20 - 5%).

Conclusion: A short anatomical distance between the esophagus and the 28mm CB is the key determinant for low LET whereas CB temperature does not predict low LET. Importantly, LET guided freeze interruption is associated with a decreased incidence of esophageal lesions.

P2433 | BEDSIDE
Conclusion:

P2434 | BEDSIDE
Cryoballoon vs. radiofrequency ablation of paroxysmal atrial fibrillation: no impact of pulmonary vein anatomy in midterm procedural success

Background: Pulmonary vein (PV) electrical disconnection is the mainstay of treatment during catheter ablation of paroxysmal atrial fibrillation (PAF). Cryoballoon (CRYO) ablation has been introduced in more recently than radiofrequency (RF) ablation, the standard technique in most centers, and head-to-head studies assessing sinus rhythm maintenance beyond 12 months are currently very scarce. PV anatomy may display anatomic variants (left common trunk and right supernumerary veins), which are thought, according to some authors, to compromise the results of CRYO.

Methods: Single-centre study, comprising 614 consecutive pts undergoing a first procedure of PAF ablation (CRYO = 287 and RF = 327 pts). Comparisons between CRYO and RF ablation were performed concerning safety and efficacy endpoints during a 12 median follow-up (IQR = 7–19).

Results: Baseline characteristics (age, gender prevalence, body mass index, AF duration, left atrial volume, left ventricle ejection fraction, CHADS2 and HAS-BLED) did not differ between groups. No differences were found regarding the number of PV at left (1.8±0.4 RF vs 1.8±0.4 CRYO; p=0.17) and right (2.2±0.5 RF vs 2.2±0.4 CRYO; p=0.10). CRYO pts presented more relapses during hospitalization (4.9% vs 9.1%; P<0.04), but use of class I or III anti-arrhythmic agents was similar. A total of 36 cases with anatomic AF were found during the 3 months blanking period (14.4% RF vs 16.7%; p=0.10) and at midterm (18.3% RF vs 17.8% CRYO; log rank p=0.25). Complication rate was similar, except for phrenic palsy that was more frequent in CRYO (2.4% vs 0.3%; p<0.02). We observed no interaction of PV anatomy on midterm procedural success: absence of a left common pulmonary trunk (log rank p=0.30); presence of right supernumerary veins (log rank p=0.33).

Conclusions: The cryoballoon performed similarly, at mid-term, to radiofrequency ablation of PAF in all different PV anatomic subsets. The presence of PV anatomic variants should not discourage the referral of patients for cryoblation of PAF.

P2435 | BEDSIDE
Radiation exposure in pulmonary vein isolation for paroxysmal atrial fibrillation: a comparison between cryoballoon ablation and 3D-mapping guided radiofrequency ablation

Background: The new development of radiofrequency-based ablation techniques renders radiation exposure an important issue in cardiac electrophysiology. Aim of the study was to evaluate the radiation exposure of cryoballoon ablation compared to the 3D-mapping guided irrigated radiofrequency ablation in patients with paroxysmal atrial fibrillation (PAF) undergoing first pulmonary vein isolation (PVI).

Methods: A total of 36 consecutive patients with paroxysmal AF were included. An esophageal temperature probe (TP) was introduced and served as LET monitor. CB freeze duration was set to 120s and premature CB freeze termination was led by LET < 15°C to avoid LET 12°C. A video recording system recorded simultaneously 28mm CB and esophagus temperatures. The shortest fluoroscopic distance between the CB and the LET probe was always measured (LAO 40°, RAO 30°) and correlated with LET. Low esophageal temperature was arbitrarily defined as LET < 25°C.

Results: Baseline characteristics were not different between both groups (Table 1). Complete PVI could be achieved in all patients. No severe adverse event occurred in both groups.

Table 1. Clinical characteristics and ablation details of patients undergoing first PVI due to paroxysmal AF

Conclusions: In PVI using cryoballoon ablation the total fluoroscopy time is twofold and the total radiation dose four times increased compared to the 3D-mapping guided irrigated radiofrequency ablation. The higher fluoroscopy time and dose in cryoballoon ablation derives from the ablation procedure when fluoroscopy is needed to verify the occlusion of the pulmonary veins before ablation.

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P2436 | BENCH
Reduction of radiation exposure in cryoballoon ablation procedures: a single center study applying intracardiac echocardiography and other radio-protective measures

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Purpose: Cryoballoon (CB) ablation has been widely adopted as a valuable alternative technique for pulmonary vein isolation (PVI) for paroxysmal atrial fibrillation (PAF). The population treated is relatively young and radiation protection is of major importance. We aimed to demonstrate, that radiation exposure can markedly be reduced by intracardiac echocardiography (ICE) and optimized settings of the X-ray system.

Methods: A total of 140 patients were studied. In 57 consecutive patients (31 male, 58±14 years, BMI 26.7±4.2 kg/m², LA 38±6.6 mm, LV EF 54.9±1.07) (group 1) undergoing CB PVI for treatment of PAF ICE was applied for transeptal puncture, confirmation of PV occlusion, guidance of wires, mapping catheters and CB and monitoring of complications. PV angiography prior to CB inflation was skipped. Thereby, fluoroscopy was avoided whenever possible. During fluoroscopy a reduced frame rate (3/s instead of 7.5/s) was chosen, distance of patient and detector was kept minimal and collimation was consequently applied. The ‘Care Position’ functionality (Siemens, Forchheim, Germany) was used to avoid fluoroscopy during table movements. Patients from group 1 were compared to 73 similar preceding consecutive patients (45 male, 58±12 years, BMI 26.5±3.8 kg/m², LA 40±3.6 mm, LV EF 55±3.3%) (group 2).

Results: No radiation exposure occurred. Total fluoroscopy time could be reduced from 18.7±6.2 to 12.1±5.5 s (p<0.001). Radiation exposure was 1652±1265 μGy*m² in group 1 compared to 5134±2451 μGy*m² in group 2 (p<0.001) Total procedure times were 108.7±23.1 min in group 1 compared to 107.0±26.5 min in group 2 (p=0.26). While total freezing time could be reduced from 2126.7±106 to 1874±414 s (p<0.01). At 6 month follow-up 74.5% vs. 81.4% (p=0.26) were free from recurrences, more patients in group 1 were followed using implantable devices (23 vs. 7%; p=0.01).

Conclusion: Radiation exposure in CB PVI could be markedly reduced without prolonging procedure times or affecting the outcome. Moreover, ICE seems to be a valuable alternative technique in PAF.

P2437 | BENCH
Reduction of radiation exposure in cryoballoon ablation procedures: a single center study applying intracardiac echocardiography and other radio-protective measures

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Conclusion: Radiation exposure in CB PVI could be markedly reduced without prolonging procedure times or affecting the outcome. Moreover, ICE seems to be a valuable alternative technique in PAF.

P2438 | BEDSIDE
Watchman LAA occlusion combined with catheter ablation is feasible in AF patients with high stroke risk and a contraindication for anticoagulation

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Purpose: Catheter ablation (CA) often relieves symptoms in drug-refractory atrial fibrillation (AF), but freedom of AF is never certain. Oral anticoagulation therapy (OAC) remains warranted in high stroke risk patients even after CA. Left atrial appendage (LAA) occlusion (LAO) is a viable alternative for prevention of thromboembolic complications in patients with 1 or more stroke risk factors. We describe a series of 64 patients where LAO was combined with CA in one single procedure.

Methods: Symptomatic patients with drug-refractory AF (CHA2DS2-VASc ≥1) and contraindication(s) for OAC were included. A pre-procedure TEE was performed to assess LAA size and anatomy, and exclude thrombus or structural cardiac abnormality. All procedures were accomplished under general anaesthesia and TEE guidance. Phased RF multi-electrode CA was carried out; PVAC PVI in PAF, and additional MASCA&MAAC CFAE ablation in PersAF. After CA, LAO was performed using the Watchman device. CA was performed under therapeutic INR and OAC was maintained the first 3 months, unless there was an absolute contraindication for OAC in which case LMWH was used for 2 weeks, followed by Aspirin and Clopidogrel. At 3 months, OAC was switched to Aspirin if LAO criteria were met on TEE. Rhythm follow-up was performed with serial ECG in all, and Holter recording at the physician’s discretion.

Results: From Sep 2009-Oct 2013, a total of 64 patients (23 female, mean age 64±8 years) underwent CA (PVI only in 45, PVI+CFAE in 19 patients) combined with LAO. The median CHA2DS2-VASC score was 3 (range 1-7). OAC contraindications were history of stroke under OAC (52%), major bleeding under OAC (14%), combination of stroke and major bleeding under OAC (9%), preference to OAC (20%), or other (5%). Watchman LAO was performed with complete acute occlusion in all, with a median number of 1 device (range 1-3). The mean total procedure time was 97±24 min, with additional 38±20 min for LAO. Adverse events during 60 day follow-up included 1 procedural major groin bleeding, and 1 device embolisation with successful groin extraction. TEE at 60 days showed that 86% of patients met all criteria for successful sealing (residual flow <5 mm), allowing them to discontinue OAC. In the remaining patients, OAC was maintained if possible until LAO was accomplished later. Complete 1 year follow-up in 41 patients showed a stroke rate of 0%.

Conclusion: LAO combined with CA for AF can be performed successfully and safely in one single procedure, with favourable effect on stroke occurrence during 1 year follow-up.

P2439 | BEDSIDE
Effect of obstructive sleep apnea on sinus rhythm maintenance in patients after ablation for paroxysmal atrial fibrillation

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Purpose: Obstructive sleep apnea (OSA) is a sleep disorder affecting many patients with atrial fibrillation (AF). OSA contributes negatively to natural history of AF, patients’ risk profile and prognosis. The aim of this study was to assess the relationship between OSA and sinus rhythm maintenance in patients after ablation for paroxysmal AF.

Methods: We enrolled 186 consecutive patients admitted to our department for paroxysmal AF ablation. Prior to the ablation procedure all patients, in addition to standard work-up, underwent a whole-night polygraphy sleep study for the diagnosis of OSA. After the procedure all patients were followed up for mean time of 36 months for the recurrences of AF, which was diagnosed when AF was detected in 24-hour ECG Holter monitoring, and/or when a patient reported symptoms of AF. OSA positive patients were those with apnea-hypopnea index of ≥5 per hour. Patients were subsequently divided into groups according to the OSA severity: mild OSA was defined as AHI between 5 and 15, moderate OSA was defined as AHI between 15 and 30 per hour, and AHI >30 per hour was the criterion for severe OSA.

Results: After excluding patients disqualified from procedure, and those with central sleep apnea, the study population consisted of 176 patients (113 (64.2%) male, mean age 58±8 years). OSA was present in 73 (41.4%) patients, while in 90 (51.1%) cases we observed recurrences of AF. It was more often in patients with than without OSA (61.1% vs. 44.2%; p=0.03). We also observed that the number of patients in whom AF was detected during the follow up period depended on severity of OSA (4% vs. 60.0% vs. 71.4%; p for trend 0.005; for non-OSA, mild, moderate and severe OSA respectively).

Conclusions: OSA is highly prevalent in patients with AF. Occurrence of OSA lowers chances on successful AF ablation. Early screening, and treatment for OSA in AF patients, may improve low success rates of AF ablation procedure.
Purpose: Atrial fibrillation (AF) refractory to medical therapy in hypertrophic cardiomyopathy (HCM) patients deteriorates the clinical status. Outcomes of radiofrequency catheter ablation (RFCA) for AF in HCM patients are controversial. We investigated the efficacy and acute hemodynamic effects of RFCA for AF in HCM patients.

Methods: We consecutively enrolled drug-refractory AF patients with HCM (HCM group, n=15) and without HCM (NHCM group, n=106). Extensive encircling pulmonary vein isolation (EEPVI) and bidirectional cavotricuspid isthmus block were performed in all patients. Left atrial (LA) pressures were measured using hemodynamic catheterization just after the trans-septal puncture and after completion of EEPVI (Pre- and post-LA pressures). We compared clinical parameters, echocardiographic parameters, electrophysiological parameters, LA pressures and recurrence rate in the both groups.

Results: The pre-LA pressures were significantly higher in the HCM than in the NHCM group (the mean pre-LA pressure: 15.6±4.8 mmHg vs. 11.5±3.3 mmHg, p<0.01). Post-LA pressures in the HCM group significantly decreased, and became similar to those in the NHCM group (Figure). No significant difference in the rate of early recurrences (within 30 days after ablation) was observed between the HCM and NHCM groups (20% vs. 5.7%, p=0.08). The rate of late recurrences (>30 days after ablation: LRs) was also similar in the both groups during a mean 436±282 days follow-up periods (LRs: 6.7% vs. 7.6%, p=0.83).

Conclusions: The LA pressure in the HCM group drastically decreased immediately after the EEPVI. The RFCA of AF was effective and safe for restoring sinus rhythm and should be considered a therapeutic option in HCM patients.

P2444 | BEDSIDE

Epicardial adipose tissue volume predicts atrial fibrillation recurrence after pulmonary vein isolation

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Purpose: Obesity is an established risk factor for atrial fibrillation (AF). It has been proposed that epicardial adipose tissue (EAT) might play a key role in promoting atrhythmogenesis due to its pro-inflammatory properties and anatomical proximity to myocardium. The aim of this study was to investigate the relationship between EAT volume and clinical characteristics and recurrence of AF.

Methods: Epicardial fat volume was computed tomography prior pulmonary vein isolation (PVI). Patients were divided into two groups according to their AF severity: 74 patients (age 56±11 yr, 60 male) had paroxysmal AF and 28 patients (age 57±10 yr, 25 male) had persistent AF. Echocardiographic parameters and C-reactive protein (CRP) levels were also assessed. Patients were followed for 3 months for AF recurrence.

Results: In comparison to patients with paroxysmal AF, patients with persistent AF had significantly higher EAT volume (109.9±28.2 vs 86.6±38.2 cm³, p<0.02).

Conclusion: Epicardial fat is associated with AF severity, LA diameter and AF recurrence after ablation. This suggests a local effect of epicardial fat tissue on the arrhythmogenic substrate promoting AF. Interventions targeting epicardial adipose tissue may be beneficial.

P2445 | SPOTLIGHT

Flow-mediated dilation is associated with cardiovascular events in non-valvular atrial fibrillation patients

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Purpose: Atrial fibrillation (AF) is associated with multiple atherosclerotic risk factors and predisposes to cardiovascular events (CVE). Endothelial dysfunction is associated with atherosclerosis and independently predicts CVE. Aim of the study was to evaluate the association between endothelial dysfunction as assessed by flow-mediated dilation (FMD) and CVE in AF patients.
Methods: We prospectively measured FMD in 514 non-valvular AF patients on anticoagulant treatment with vitamin K antagonists. Patients were followed-up for a mean time of 23.5 months. The main composite outcome of the study was the occurrence of ischemic events in the coronary and cerebral circulation.

Results: Mean value of FMD was 5.08±4.33%. A CVE occurred in 44 patients (8.5%). Atrial fibrillation (AF) induced significant reduction in oxygen consumption rate (OCR) at maximal respiration (451.5±5.15 vs. 272.7±22.4 pmol/min; control vs. irregular paced; p<0.05). The mitochondrial spare respiratory capacity was also reduced in irregular paced heart (141.3±53.3 vs. -0.25±27.5 pmol/min; control vs. irregular paced; p<0.05). Consistent with this, isolated heart studies, short term irregular pacing in sheep also reduced left ventricular contractility (±dp/dtmax, pre 2295±830 vs post 1030±114 pmh/g, p<0.05) and reduced relative phosphophorylation of phospholamban (cont 1.12, paced 0.9 ADU, p<0.05).

Conclusions: Irregular ventricular rhythm in the context of AF induces fundamental changes in mitochondrial function and significant gene expression changes of key proteins involved in calcium handling. As such, AF induced depression of mitochondrial function would be expected to accentuate the progression of HF. The precise mechanism of AF induced mitochondrial dysfunction requires further investigation.

P2448 | BEDSIDE
Atrial rhythm pattern of dissociated pulmonary venous activity is the novel characteristics of the triggering ectopy for atrial fibrillation
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Background: Pulmonary veins (PVs) play an important role in the arrhythmogenesis of atrial fibrillation (AF). Rapidly firing ectopic foci in PVs have been shown to be the triggers for AF. Radiofrequency (RF) energy ablation can be delivered at the PV ostium with the endpoint of distal PV disconnection. After PV isolation, isolated intrinsic ectopic beats are sometimes recorded on circular mapping catheter. This dissociated PV activity (DPVA) could be the remaining foci of atrial ectopies, which has not been demonstrated.

Objective: We hypothesized that DPVA could be the trigger ectopy and examined the concordant ratio of the localization and pattern of DPVA with those of trigger ectopy. The localization was determined among 4PVs. The pattern was determined as (1) isolated ectopic beats, (2) regular ectopic rhythm, or (3) fibrillation.

Method and results: This is a single center prospective study. We defined trigger ectopy as the documented ectopic foci that spontaneously initiated AF when early molecular changes in pAF lead to microRNA (miRNA)-mRNA dysregulation. Performing state-of-the-art transcriptomic studies in order to test the hypothesis that early molecular changes in pAF lead to microRNA (miRNA)-mRNA dysregulation which further drives AF progression.

Purpose: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, yet there are no effective pharmacologic treatments, underscoring a lack in the current understanding of the molecular mechanisms of AF. Using atrial samples from patients with paroxysmal AF (pAF) or in normal sinus rhythm (SR), we performed a high-throughput state-of-the-art transcriptomic studies in order to test the hypothesis that early molecular changes in pAF lead to microRNA (miRNA)-mRNA dysregulations which further drives AF progression.

Methods: High quality total RNA including miRNA was isolated from atrial biopsies of age-matched and sex-matched pAF and SR patients (n=6-8 per group). The average time before last episode of AF in the pAF group was 2 days. A portion of the RNA was used for miRNA microarray while another portion from the same or similar samples was used for RNA-sequencing. Putative targets of miRNAs were searched using TargetScanHuman2.2 while functional annotation clustering was performed using DAVID.

Results: RNA-sequencing identified 177 genes that are differentially expressed in pAF patients (P<0.05), including some involved in immune response. Meanwhile, miRNA microarray identified 49 miRNAs that are both differentially expressed in pAF versus SR patients. Functional annotation clustering revealed that early molecular changes in pAF lead to microRNA (miRNA)-mRNA dysregulations which further drives AF progression.

Purpose: Identification of microRNA-mRNA dysregulations that drive the development of atrial fibrillation
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Objectives: Our group performed state-of-the-art transcriptomic studies in order to test the hypothesis that early molecular changes in paroxysmal atrial fibrillation (pAF) lead to microRNA (miRNA)-mRNA dysregulations which further drives AF progression.

Methods: High quality total RNA including miRNA was isolated from atrial biopsies of age-matched and sex-matched pAF and SR patients (n=6-8 per group). The average time before last episode of AF in the pAF group was 2 days. A portion of the RNA was used for miRNA microarray while another portion from the same or similar samples was used for RNA-sequencing. Putative targets of miRNAs were searched using TargetScanHuman2.2 while functional annotation clustering was performed using DAVID.

Results: RNA-sequencing identified 177 genes that are differentially expressed in pAF patients (P<0.05), including some involved in immune response. Meanwhile, miRNA microarray identified 49 miRNAs that are both differentially expressed in pAF versus SR patients. Functional annotation clustering revealed that early molecular changes in pAF lead to microRNA (miRNA)-mRNA dysregulations which further drives AF progression.

Conclusions: To the best of our knowledge, this is both the first transcriptomic analysis and miRNA microarray study using samples from pAF patients. By intersecting results from these two parallel studies, we provide novel insights into the mechanism of AF development.
the miRNA-mRNA regulations that may drive the progression of AF to more persistent forms, via transcriptional dysregulations. This may open new avenues of investigation into AF pathogenesis and the development of novel therapeutics.

**P2450 | BEDSIDE**
The role of preoperative administration of L-carnitine in the prophylaxis of post CABG atrial fibrillation
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**Purpose:** Atrial Fibrillation (AF) is one of the most common complications in patients who undergo coronary artery bypass grafting (CABG) surgery. The reported incidence of postoperative AF ranges from 40% post- CABG. L-carnitine can cause atrial pump dysfunction resulting in ventricular filling impairment with an increase in the incidence of heart failure and development of stroke, thus contributing to the rise of post-CABG disability and mortality. The aim of this study was to evaluate the effect of L-carnitine administration on postoperative AF following CABG surgery.

**Methods:** Two hundred and fifty patients undergoing elective CABG surgery, without history of AF or previous L-carnitine treatment, were enrolled and randomly assigned to a L-carnitine group (L-carnitine 3000 mg/d, n=125) or a control group (Placebo, n=125) starting 2 days preoperatively and continuing for 2 days after surgery. The primary endpoint was the occurrence of postoperative AF. C-reactive protein (CRP) levels were assessed in all patients by means of high sensitive CRP kits before surgery as baseline levels and 48 hours postoperatively. Results: The incidence of AF was 15.4% in our population. L-carnitine significantly reduced the incidence of postoperative AF (7.5% in L-carnitine group versus 19.4% in placebo; P=0.043) and postoperative CRP level versus placebo (8.79±6.9 versus 10.83±5.7; P=0.021).

**Comparison of patients' demographic data**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>54</td>
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</tr>
<tr>
<td>Male</td>
<td>13</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>60.01±9.23</td>
<td>59.88±7.98</td>
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<tr>
<td>Ejektion fraction</td>
<td>45.37±8.80</td>
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</tr>
<tr>
<td>Family history</td>
<td>31.3%</td>
<td>34.3%</td>
<td>0.009</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>34.3%</td>
<td>41.6%</td>
<td>0.374</td>
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<tr>
<td>Hypertension</td>
<td>62.7%</td>
<td>59.7%</td>
<td>0.723</td>
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<td>Hypothyroidia</td>
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<td>47.8%</td>
<td>0.604</td>
</tr>
<tr>
<td>Previous MI</td>
<td>18.2%</td>
<td>22.4%</td>
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</table>

**Conclusion:** Our study revealed that L-carnitine administration before CABG surgery may inhibit and reduce the incidence of post-CABG AF and so its complications.

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**P2451 | BENCH**
Exploring the role of Pitx2 and candidate genes in human and murine atrial tissue
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Genome-wide association studies (GWAS) have found polymorphic loci on Chromosome 4q25 that associate with atrial fibrillation (AF). The closest gene to these loci is the Paired-like homeodomain transcription factor 2 (Pitx2). Pitx2c is the predominant isoform in the heart. We have shown that heterozygous Pitx2c+/− mice are more susceptible to AF and that Pitx2c is more highly expressed in the left atrium (LA) than the right atrium (RA) in mice and patients. We measured mRNA and protein expression levels of candidate genes generated by gene arrays in Pitx2c−/− mouse atria, in human and murine atrial tissue.

We studied LA and RA from 36 mice (18 Pitx2c−/−, 18 littermate WT, 14-20 weeks) and from patients in sinus rhythm (n=7; chronic (n=13) and paroxysmal AF (n=13), all undergoing open heart surgery (CABG or valve surgery, mean age 70). Transcript levels of candidate genes were quantified by RT-PCR and protein levels were quantified by western blot relative to calnexin protein expression. LA mRNA levels of Cc21l1, Ddfl1, Phlda1, Ppp1rb, Scar5, Tnml2, and Cxcl14 were higher in RA than in WT and Pitx2c−/− mice, Cc21l1 and Ddfl1 mRNA was higher in Pitx2c−/− LA compared to WT LA (p<0.006; p<0.0385, respectively). In patients, Cc21l1 and Pitx2c mRNA was higher in LA than in RA, chronic AF and paroxysmal AF groups (Cc21l1 p=0.000, p=0.001, p=0.014; Pitx2c p=0.017, p=0.000, p=0.000, respectively). Further, Ddfl1 and Ppp1rb were expressed at lower levels in the LA of patients with chronic AF compared to those in SR (Ddfl1 p=0.044, Ppp1rb p=0.008). Cc21l1 was expressed at lower levels in the LA of patients with AF compared to the LA of patients in SR (p=0.05).

PITX2 protein levels in mice were higher in LA than in RA (p<0.005; 8 WT and 8 Pitx2c−/− mice in Pitx2c mRNA, but no protein expression in mice. Human PITX2 protein expression in LA and RA was heterogeneous and was neither related to SNP status of rs2200733 and rs6838973, nor different in LA and RA.

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**P2454 | BEDSIDE**
Correlation between atrial fibrillation cycle length and fractionation as a predictor of long-term atrial fibrillation free survival
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**Purpose:** Fractionation of electrograms is associated with local fibrosis but can also occur during functional conduction block. We hypothesized a differentiation between structural and functional fractionation can be a predictor of atrial fibrillation (AF) free survival. The aim of this study was to assess the potential value of a mean atrial fibrillation cycle length (AFCL) to fractionation correlation coefficient as a predictor of AF free survival after pulmonary vein isolation (PVI).

**Methods:** 28 patients with “lone” AF planned for PVI were included. A steerable twopolar catheter with 5 splines (PentaRay, Biosense Webster) was inserted in the left atrial appendage. During AF, 10 bipolar electrograms (EGMs) were recorded during 15 seconds. AFCL was determined manually, a fractionation score was calculated automatically using criteria based on complex fractionated atrial EGMs criteria. Receiver operating characteristic curve analysis was
performed to define the optimal cut-off value for mean AFCL to fractionation correlation coefficient (AFCC). Median follow-up was 73 months.

**Results:** Mean age was 53 years and 86% had paroxysmal AF. Mean AFCL was 171 ms, mean fractionation score was 10 activations per second. Mean AFCC was -0.324. Eighteen patients were free of AF at the end of the study period. The AFCC was significantly higher in patients who were free of AF compared to patients who were not (z = -0.478 vs z = -0.049, p = 0.001). The AFCC predicted long-term AF free survival with an accuracy of 96% (p < 0.001). With a cut-off of -0.170, the sensitivity was 90% and the specificity was 100%.

**Conclusion:** In the present study, the mean AF cycle length to fractionation correlation coefficient was significantly associated with long-term AF free survival and can potentially be used as a predictor of long-term AF free survival after ablation.

**P2455 | BEDSIDE**

Characterization of signal-averaged vector-projected high resolution eeg and genetic polymorphisms of scnsa in brugada syndrome

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**Purpose:** Brugada syndrome is associated with a high risk of lethal arrhythmias, potentially caused by mutations in the SCNSA genes that encode a subunit of the cardiac sodium ion channel. In this study, we verified the characterization of morphology of precordial V1-2 in 12-Leads ECG, late potentials (LPs), interlead difference of activation recovery time by 178 high-resolution ECG and genetic polymorphisms of SCNSA genes.

**Method:** We used originally developing 187-ch signal-averaged vector-projected high resolution ECG (DREAM-ECG) that can evaluate 12-leads ECG and abnormalities of ventricular depolarization and repolarization. This DREAM-ECG consisted of an input box with high resolving power amplification, vector-projected matrix lead synthesizer, and data handling section. We recorded 10 minute of body surface ECG by using Mason-Likar lead system at resting supine position. Synthesized 187-ch ECG based on vector-projection theory was generated. The existence of LP was defined by the LAS40 ≥44ms and IQRS ≥127 ms on signal averaged XYZ leads ECG. The values for the mean activation recovery time (RT) dispersion were automatically calculated by the mean difference between the greatest RT interval (RTmax) and the smallest RT interval (RTmin). Corrected RT intervals were calculated by Bazett’s formula. Genetic screening for 11 mutation sites of SCNSA was performed in 40 patients with Brugada like ECG.

**Results:** 12-Lead ECG revealed 10 covered type, 30 saddle-back type ECG. The value of RT dispersion was higher in BrS with covered type than those in saddle-back type (40.5±2 vs. 29.3±2.3 ms, p<0.05). The existence of LP was not significantly different between saddle back type and covered type (16/30 vs. 7/10, ns). Missense mutations were detected 8 samples of H558R, 5 samples of R191Q and 2 samples of P1090L. In the context of genetic polymorphisms of SCNSA and DREAM-ECG, H558R hetero mutation was identified in 6 out of 10 Brugada syndrome patients. The 12-LCG morphology of 4 patients with R191Q and 2 patients with P1090L were saddle-back type. The 21 patients out of 27 patients with no mutation demonstrated saddle-back type on 12L-ECG.

**Conclusion:** Signal-averaged vector-projected high resolution 187-ch ECG and the SCNSA mutation may provide a new insight for risk stratification in patients with Brugada syndrome.

**P2456 | BEDSIDE**

Periodic repolarization dynamics predicts mortality in diabetic post-infarction patients

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**Purpose:** Periodic repolarization dynamics (PRD) refers to low frequency cyclic changes of repolarization instability related to sympathetic nerve activity. Diabetic post-infarction patients can suffer from regional inhomogeneities of automatic innervation which may contribute to increased vulnerability to malignant tachyarrhythmias and which may be captured by PRD. Moreover, SCNSA mutation of 983 survivors with acute myocardial infarction (MI). Within the 2nd week after MI, a 30 minute high resolution ECG was performed in Frank leads configuration under standardized conditions. PRD probes the spectral power of spatiotemporal variations of repolarization in the low frequency range (<0.1Hz). In previous studies, PRD was a very strong predictor of mortality in diabetic patients with 5.4% in patients with normal and abnormal PRD, respectively (p<0.001). Multivariately, abnormal PRD was the strongest predictor of mortality in diabetic patients (hazard ratio 5.7 (95% CI 2.3-14.0), p<0.0001) outperforming reduced LVEF <35% (1.3 (0.5-3.2), p=0.606).

**Conclusions:** Increased PRD identifies diabetic post-infarction patients at very high risk of subsequent death. Future studies are needed to test whether these patients benefit from prophylactic therapies.
P2429 | BENCH

A CNS cell group that controls electrical stability of the heart

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Introduction: Electrical stimulation of the vagus nerve has been shown to protect against ventricular tachyarrhythmia (VT). The exact mechanism of this effect is unknown. It also remains unclear whether acute or chronic withdrawal of tonic vagal efferent activity to the heart predisposes the heart to VT. We used triple-surgical preparations on a C57/10 background as a model of autonomic dysfunction associated with sustained reduction in vagal tone, while in a rat model we genetically targeted vagal preganglionic neurones in the dorsal motor nucleus of the vagus nerve (DVMN) for their selective acute silencing using a pharmacogenetic approach.

Methods: In 12 male Sprague-Dawley rats (380-420g), lentiviral vectors were used to transduce DVMN neurones to express an inhibitory Gi-protein-coupled Drosophila allatostatin receptor (Alstr) or GFP control. Applying allatostatin peptide rapidly silenced transduced neurones. To investigate the role of age-dependent autonomic dysfunction, young (2-3 months) and old (12-16 months) TKO and wild type (WT) mice were used. Anaesthetised with urethane (1.3g/kg, i.p.), an octopole electrode catheter was inserted into the jugular vein and advanced into the right atrium and ventricle. The animals underwent programmed electrical stimulation of the right ventricle to obtain ventricular effective refractory period (VERP). Ventricular tachycardia (VT) inducibility by burst pacing was also assessed.

Results: Acute inhibition of the DVMN vagal preganglionic neurones in rats resulted in reduced VERP (34.0±6.5 ms vs 21.4±3.3 ms, p=0.009) and shorter cycle length when burst pacing cycle was required to induce ventricular tachyarrhythmia (46.3±6.5 ms vs 21.4±3.3 ms, p=0.009). Young TKO mice showed no difference in VERP (37.0±5.2 ms vs 37.0±3.1 ms, p=0.09). However, in older TKO mice there was a reduction in VERP (38.6±8.0 ms vs 43.3±13.1 ms, p=0.001). Systemic administration of methyl atropine (1mg/kg, i.p.) to WT mice mimicked the pro-arrhythmic phenotype of synuclein deficiency.

Conclusion: This study demonstrates that decreased activity of a distinct population of vagal preganglionic neurones predisposes the heart to ventricular arrhythmia by reducing the effective refractory period. We hypothesise that CNS disorders associated with autonomic dysfunction (modelled here by global synuclein deficiency) and decreased DVMN activity may lead to a pro-arrhythmic phenotype.

P2461 | BENCH

Effects of the site of origin and coupling interval of premature ventricular depolarizations on the hemodynamic and mechanical response in pigs with and without pacing-induced cardiomyopathy


Purpose: Frequent premature ventricular depolarizations (VPD) can cause or worsen a previously acquired cardiomyopathy. This effect has been associated with the burden of VPD. However, its mechanism remains unknown. The aim of this study was to analyze the acute hemodynamic and mechanical effects of VPD arising from different ventricular sites at different coupling intervals (CI) in normal and cardiomyopathic pig hearts.

Methods: Four control pigs with normal hearts and four with pacing-induced cardiomyopathy (CM) were studied. Echocardiographic measurements were used to validate the animal model. VPDs were performed at decreasing Ci from 16 left (8 epicardial and 8 endocardial) and 3 right ventricular sites. Left ventricular (LV) and right ventricular (RV) pressure, arterial pressure, aortic blood flow (ABF) and the ECG were continuously recorded.

Results: A total of 608 VPDs were evaluated. No hemodynamic or mechanical differences between epicardial and endocardial locations were noticed. A deleterious effect on ABF and maximum LV dp/dt associated with shorter coupling intervals was found (p<0.001), and this was more prominent in the CM group (p<0.001). All VPDs at 500 ms CI in the control group generated ABF, but 22% in the CM group did not (p<0.001). VPD that did not generate ABF (non-flow VPD) were significantly increased at decreasing CI in both groups (p<0.01) with a more manifest effect on the CM animals (23.9% vs. 44.3% at 450 ms CI, p<0.05). At very short CI, differences between the groups tended to disappear. The regional analysis (8 LV regions [epicardial + endocardial] and 3 RV regions) showed that at 450 ms CI, only the anterolateral basal and medial regions of the LV generated more than 25% non-flow VPD in the control group, whereas, in the CM group, all regions generated more than 25% non-flow VPD.

Conclusions: The coupling interval of premature ventricular depolarizations plays a major role in their deleterious effect on the heart. In addition, based on the rate of non-effective beats, the site of origin may also be critical. Remarkably, extrastolic beats have a more detrimental effect on cardiomyopathic rather than in normal hearts.

P2462 | BENCH

Defibrillation threshold of ventricular fibrillation in a porcine model of mild therapeutic hypothermia

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Purpose: Mild therapeutic hypothermia (MTH) is being used in post-resuscitation care for its anticipated neuroprotective effect. The relation between MTH and malignant ventricular arrhythmias has not been exactly clarified. The aim of the study is to compare defibrillation threshold of ventricular fibrillation before and after induction of MTH in whole body porcine model.

Methods: Veno-arterial extracorporeal membrane oxygenation (ECMO) with cooling circuit was introduced in fully anesthetized pigs (n=10) for temperature management and myocardium protection. Ventricular fibrillation (VF) was provoked by ventricular rapid pacing each three times during normothermia and after reaching the target temperature (32 degrees Celsius in the pulmonary artery). The transcutaneous defibrillation threshold was estimated as the lowest energy of biphasic shock (70-100-150-200-270 J gradually) which terminated VF.
Results: Defibrillation threshold of VF in normothermia was 270 (IQR 188; 270) J as compared during maintaining of MTI 150 (150; 270) J, p<0.001. Also the number of shocks necessary to terminate VF was during MTI lower than in normothermia - 3 (3; 5) vs. 5 (4; 5), p<0.001.

Conclusions: Defibrillation threshold of VF in a whole body porcine model is during MTI lower than in normothermia condition.

CLINICAL OUTCOMES IN ATRIAL FIBRILLATION I

P2464 | BEDSIDE
Daily physical activity and risk of atrial fibrillation

Vigorous exercise and endurance training increase the risk of atrial fibrillation (AF). The association between daily physical activity (PA) during leisure time and work with the risk of AF is largely unexplored. The aim of the present study was to investigate the association between the level of daily PA and the risk of AF in a large cardiovascular longitudinal study, the 60 years old men and women from our city.

A cohort consisting of every third man and woman reaching the age of 60 in our large city living in 1997-1999 were included. Accelerometric records, an ECG, and blood samples were collected at baseline. PA was classified in four different categories: during leisure time as sedentary (I), <2h/week; mild (II), <8h/week; moderate (III) regular motion - 30 min 2-3 times/week and sustained (IV) as regular training 3 times/week. Correspondingly, PA during working hours was graded according to the intensity of the work as very mild (I), mild (II), intense (III), very intense (IV) and to the time spent sitting at work as always sitting (I), sitting less than half day (II), sitting less than half day (III) and never sitting (IV).

Incident cases of AF were ascertained via the Swedish national hospital discharge register. Risk of AF was calculated by Cox regression and expressed as hazard ratio (HR) with 95% confidence intervals (CI) at the univariate analysis and after adjustment for sex, hypertension, diabetes, smoking, obesity, left ventricular hypertrophy, previous myocardial infarction.

During 12 years of follow up AF incidence rate was 4.4/1000 person-years. Leisure-time PA showed a U-shaped relationship with the risk of AF, with a trend toward increased risk in group I (HR 1.22; 95% CI 0.91-1.63); and IV (HR 1.54, 95% CI 0.97-2.45) as compared to group II and III, in the fully adjusted model. We observed a 37% reduction in AF risk in HR (0.63, 0.42-0.94 (95%CI) in the fully adjusted model, in individuals physically active during working hours as compared to those sitting all the time at work. The intensity of work was not associated with AF risk neither at the univariate (HR 0.82 and 95% CI (0.45-1.48)) nor at the multivariate analysis [HR 0.68 95%CI (0.37-1.25)].

The results suggest a possible U-shape relationship between leisure time PA with trends toward higher risks both in those with low PA as well as in those with regular PA. Due to the close relationship between daily and weekly PA, it is not possible to determine whether PA during leisure time can be considered as a risk factor for AF. A clear need for further research with more refined questionnaires on PA is needed.

P2466 | BEDSIDE
Utility of non-invasive assessment of left atrial function and diastolic filling parameters in predicting recurrence of atrial fibrillation following catheter ablation

Purpose: Unfavorable left atrial (LA) remodeling increases the risk of atrial fibrillation (AF) after catheter ablation (CA). However, specific measures of LA function that could predict occurrence of AF recurrence are poorly defined.

Methods: Patients (pts) who underwent CA for AF between September 2008 and September 2010 were included. A transesophageal echocardiogram was performed at baseline, at 24 hours after CA and at 3 months. Peak longitudinal strain of the inferior LA wall was measured during atrial contraction (LAA strain) and LAa strain was defined as change in strain from baseline to 24 hours. AF recurrence was defined as atrial activity captured by electrocardiogram. The Cox proportional hazards model was used to investigation the relationship between clinical and LA variables and AF recurrence.

Results: A total of 175 pts (135 male, 62±11 years) were included. Baseline LA strain was -17±5. LA strain decreased 24 hours after ablation (mean ±SD LAa strain 4±6). Early recurrence of AF (<3 months) was documented in 54 pts (31%). Persistent AF was the strongest predictor of early AF recurrence (hazard ratio (HR)=2.85, P=2.9e-4), followed by lower baseline total LA emptying fraction (HR=0.96, 1.8e-4), higher diastolic pulmonary vein inflow (HR=30.61, P=2.1e-4) and higher early diastolic (E) mitral inflow (HR=10.37, P=3.4e-4) velocities.

Baseline LA strain and LAA strain were not associated with early AF recurrence. Of the 108 patients with long-term follow-up (26±13 months), late AF recurrence was documented in 44 pts (41%). In contrast to early AF recurrence, a larger LAa strain was associated with risk of late AF recurrence (mean 5.9 vs 1.9, HR 1.11, P=0.018). Other measures of LA function, including baseline LA strain and total LA emptying fraction, were not associated with late AF recurrence. Early AF recurrence was a stronger predictor of late AF recurrence (HR=2.6, P=0.0019).

Conclusion: Non-invasive measures of LA function and diastolic parameters before and following CA may be useful in predicting early and late recurrences of AF. These data are easily obtained and may be helpful in guiding management following CA.

P2467 | BEDSIDE
Sex- and age-stratified 20-year changes in the prevalence of atrial fibrillation in general population
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Purpose: Atrial fibrillation (AF) has increased globally and is believed to increase in the future; therefore, we analysed its prevalence in the recent 20 years.

Methods: We analysed the large annual health check-up database with annual 12-lead electrocardiogram (ECG) results of the residents in our prefecture. AF was diagnosed using ECGs of 3,127,123 participants aged 50–79 years (64.6±7.5; years; men, 36.8%) during 1993–2012. The prevalence of AF was sex- and age-stratified (50–59, 60–69 and 70–79 years). Mitral inflow velocity was assessed by Doppler echocardiography. The Cox proportional hazards model was used to perform the multivariate analysis including age, height, blood pressure, smoking, alcohol consumption and diabetes mellitus as risk factors for incident AF in 2012 in those without AF in 2007.

Results: AF prevalence peaked in 2007 (3.41%, 2.06% and 0.76% for men aged 50–59 years) and 2006 (3.41%, 2.06% and 0.76% for women aged 50–59 years). There was a significant decrease in AF prevalence in both men and women from 2007 to 2012 (p<0.05).

Conclusion: AF prevalence peaked in 2007 (3.41%, 2.06% and 0.76% for men aged 50–59 years) and 2006 (3.41%, 2.06% and 0.76% for women aged 50–59 years). There was a significant decrease in AF prevalence in both men and women from 2007 to 2012 (p<0.05).

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in BMI in women aged <70 years. However, the mechanism of this decrease remains unclear.

P2468 | BESIDE
Incidence of hospitalization for heart failure in patients with paroxysmal and sustained type of atrial fibrillation: one-year follow-up of the Fushimi AF Registry
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Purpose: There is well-documented relationship and complex interaction between AF and heart failure. However a relationship between heart failure and the types of AF (paroxysmal, persistent or permanent) AF is unknown.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku, Fushimi-ku is densely populated with a total population of 283,000, and is assumed to represent a typical urban community in Japan. At present, we have enrolled 3,821 patients (1.4% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,966 patients as of December 2013. We compared the baseline clinical characteristics and one-year outcomes in patients with paroxysmal AF (P AF; n=1,398, 47.1%) and those with sustained (persistent or permanent) AF (SAF; n=1,568, 52.9%).

Results: Patients with PAF were younger (P AF vs. SAF: 72.6 years vs. 75.0 years of age; p<0.01) and had less co-morbidities and thus had lower CHADS2 score, compared with those with SAF. Patients with PAF had lower risk of hospitalization for heart failure. (n=20 vs. 26) (1.4% vs. 1.7%; p=0.62) between PAF and SAF. In patients with PAF, the incidence of hospitalization for heart failure was less (n=40 vs. 81) (2.9% vs. 5.2%; p<0.01). After the adjustment by age and gender in multiple logistic regression models, PAF was independently associated with the incidence of hospitalization for heart failure (adjusted odds ratio, 0.59, 95% confidence interval, 0.39 to 0.86; p<0.01). Conclusion: Patients with PAF were younger, had less co-morbidities and thus had lower CHADS2 score, compared with those with SAF. During the one-year follow-up period, there was no difference in stroke between PAF and SAF, but AF patients with PAF had lower risk of hospitalization for heart failure.

P2469 | BESIDE
Is cardiovascular death a primary driver of mortality in higher age groups of patients with non-valvular atrial fibrillation? Results from the GARFIELD Registry
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Purpose: To investigate the influence of age on baseline characteristics and clinical outcomes in patients with non-valvular atrial fibrillation (AF).

Methods: In the ongoing, international registry, GARFIELD, a total of 12,458 prospective patients were enrolled at 739 sites in 30 countries between March 2010 and January 2013. Results are reported at 1-year follow-up.

Results: A total of 29.2%, 31.9% and 38.9% of patients were aged <65 years, 65–74 years and ≥75 years, respectively. Increasing age was associated with a higher rate of comorbid conditions. Oral anticoagulant (OAC) use increased proportionately with age, and antiplatelet (AP) therapy was used more often in patients <65 years. The unadjusted event rates of stroke/systemic embolism (SE), major bleeding and mortality increased by 2.5-, 3- and 4-fold, respectively, in patients aged ≥75 years compared with those <65 years. In patients aged ≥65 years, cardiovascular (CV) death accounted for less than half the rate of all-cause death.

Conclusion: Increasing age was associated with higher risk of stroke/SE, death and major bleeding events in patients with non-valvular AF. CV-related death was not the main cause of death in patients ≥65 years.

P2470 | BESIDE
High level of HbA1c predicts ablation outcome in patients with paroxysmal atrial fibrillation and type 2 diabetes mellitus
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Purpose: Type 2 DM was associated with higher risk of AF. Whether the level of HbA1c affects the radiofrequency catheter ablation outcome is unknown. The aim of this study is to evaluate whether the baseline level of HbA1c could predict procedural outcome in patients with paroxysmal AF and type 2 DM who undergoing catheter ablation.

Methods: One hundred forty nine patients were selected for the study and their baseline level of HbA1c was evaluated before ablation. All the patients underwent pulmonary vein antrum isolation and extensive follow-up by ECG, Holter and office visit.

Result: Out of 149 patients, 60 (40.3%) patients developed recurrence after average follow-up of 14.1±10 months. Baseline level of HbA1c was higher in recurrent patients than that of patients remained arrhythmia free (HbA1c =7.18±1.12% vs. 6.85±1.12%; p<0.01). After adjusting for age, gender and duration of DM, left atrium size (HR =1.10, p=0.001) and HbA1c (HR =1.12, p=0.016) was found to be a significant predictor of recurrence. The receiver operating characteristic (ROC) analysis of multivariable prediction model showed that an HbA1c cut-off value ≥6.85% predicted recurrence with 55.0% sensitivity and 67.4% specificity (AUC=0.634, figure left). The success rate was in 69.0% in <6.85% and 46.8% in ≥6.85% group (log-rank p=0.004, figure right).

Conclusion: The high level of HbA1c is associated with an increased risk of recurrence of atrial tachyarrhythmia in patients with PAF and DM who undergoing catheter ablation.
cardiovascular (CV) mortality and morbidity. Despite the association with arterial hypertension is well established, to date the knowledge of factors influencing AF development is incomplete, especially in sub-populations at high risk. Accordingly, we analyzed characteristics and risk factors in patients participating to Campania-Salute Network (CSN) registry, to investigate frequency and determinants of AF development.

Methods: From the CSN, we selected 6905 hypertensive patients (52±12 years, 57% men, 5% diabetic, 41% obese), without history of AF, prevalent CV disease and with left ventricular (LV) ejection fraction >50%, and no more than stage III CKD (by simplified MDRD).

Results: During follow-up (median 47 months, inter-quartile range 10-71 months) a first AF episode occurred in 107 patients (rate of 4/1000 patients/year). In exploratory statistics, patients who developed AF (AF group) were older, and exhibited higher body mass index (BMI), heart rate and systolic blood pressure (BP) both at baseline and at the time of the last available visit (all p<0.01), than patients who did not develop AF (no-AF group). They also had higher ejection fraction, higher LV mass and mitral peak-E velocity, and larger left atrial (LA) diameter (all p<0.001). At baseline, AF group was taking more medications (p<0.001) due to more frequent prescription of diuretics (p<0.005), ACE inhibitors (p<0.002), ß-blockers (p<0.02) and Ca++ channel blockers (p<0.001). Cox regression by a backward building procedure including all covariables that were significantly differ- ent between the two groups demonstrated significant hazard ratios for older age (HR=1.03, 95% CI 1.03-1.13; p=0.001), higher number of antihypertensive meds (HR=1.48; CI: 1.17-1.86; p<0.001), enlarged LA diameter (HR=1.03/cm m-1; CI: 1.01-1.05; p=0.003), and less use of diuretics (HR=0.52; CI: 0.28-0.96; p<0.04).

Conclusions: higher BMI, larger LA diameter, and increased need for more medications are characteristics of an hypertensive phenotype at high risk for incident AF. Identification of the risk of incident AF in arterial hypertension may allow to better modulate antihypertensive therapy for prevention. Our analysis suggests that diuretics, helping both control of BP and atrial wall stretching, might have a role in prevention of AF in high risk individuals.

P2472 | SPOTLIGHT
Brady-tachy sinus node disease after atrial fibrillation ablation
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Purpose: Brady-tachy sinus node dysfunction (SND) is commonly associated with persistent atrial fibrillation (AF), but it is often unidentified during arrhythmia. We prospectively studied patients with persistent and long standing persistent AF referred to our centre for transeptal catheter ablation to detect clinical characteristics predictive of underlying SND.

Methods: From January 2007 to November 2013 we enrolled patients with persistent AF with indication to transcatheter ablation. They underwent AF ablation by pulmonary vein (PV) isolation and linear lesions with nonfluroscopic navigated higher body mass index (BMI), heart rate and systolic blood pressure (BP) both at baseline and at the time of the last available visit (all p<0.01), than patients who did not develop AF (no-AF group). They also had higher systolic blood pressure (p<0.001), enlarged LA diameter (HR=1.03/cm m-1; CI: 1.01-1.05; p=0.003), and less use of diuretics (HR=0.52; CI: 0.28-0.96; p<0.04).

Conclusions: higher BMI, larger LA diameter, and increased need for more medications are characteristics of an hypertensive phenotype at high risk for incident AF. Identification of the risk of incident AF in arterial hypertension may allow to better modulate antihypertensive therapy for prevention. Our analysis suggests that diuretics, helping both control of BP and atrial wall stretching, might have a role in prevention of AF in high risk individuals.

P2473 | BEDSIDE
Atrial fibrillation in first acute myocardial infarction
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Purpose: To compare the risk factors and in-hospital outcome in patients who developed Atrial Fibrillation during first acute myocardial infarction (AMI) compared to those in Sinus Rhythm (SR).

Methods: 12871 patients with first AMI admitted (January 1991 to December 2012) were divided into 2 groups, (AF) Group: 227 (1.8%) and Sinus Rhythm (SR) Group, 12644 (98.2%).

Results: The overall age was 59±12 years, but AF Patients were older (65±12 years vs. sinus rhythm 53±12 years p<0.001). Female gender, diabetes and hypertension were more common in AF group respectively as compared to SR Group p<0.001 for all. On the other hand, Smoking and Dyslipidemia were more frequent in SR Group, p<0.001 and p<0.002 respectively. Arteries were 156 (88.7%) in AF Group and 9023 (91.7%) in SR Group p<0.001. Asians were 5985 (47.3%) in SR Group and 48 (21.1%) in AF Group p<0.001. Mean cholesterol, LDL and TG were higher in AF Group as compared to SR Group p<0.001. In-hospital mortality was higher in AF Group as compared to SR Group. In-hospital mortality was 46 (20.3%) in AF Group and 84 (7.1%) in SR Group p<0.001. VF occurred more frequently in AF Group 65 (28.6%) vs. 131 (1%) in SR Group p<0.001. CVA occurred in 5 (2.2%) patients in AF Group and 54 (0.4%) patients in SR Group p<0.001. Congestive heart failure occurred 659 (5.1%) patients 31 (12.2%) in AF Group and 628 (5%) in SR Group p<0.001. Ejection Fraction<35% was seen in 35 (15.4%) in AF Group and 874 (6.8%) in SR Group p<0.004. Mean hospital stay was 7±5 days for AF Group and 5±3.5 days for SR Group p<0.001.

Conclusion: Patients having AF are more likely to be diabetic and hypertensive as compared to patients in sinus rhythm. AF in First AMI was associated with more in-hospital mortality, mechanical and electrical complications as compared to patients in sinus rhythm.

CLINICAL OUTCOMES IN ATRIAL FIBRILLATION II
P2475 | BEDSIDE
Predictors of mortality in patients with persistent atrial fibrillation: role of chronic kidney disease
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Background: Chronic Kidney Disease (CKD) is associated with increased cardiovascualar mortality. Its association with survival in subjects with Atrial Fibrillation (AF) has not been described.

Methods: Subjects with persistent AF undergoing elective electrical cardioversion from 1/2000 to 12/2005 at our clinic were followed for mortality through 12/2008. Renal function was assessed at time of cardioversion and defined based on estimated glomerular filtration rate (GFR); A GFR<60 ml/min/1.73m2 was considered normal, GFR 40-60 ml/min/1.73m2 as moderate CKD, and GFR<40 ml/min/1.73m2 as severe CKD. Kaplan-Meier method assessed mortality. Groups were compared using the log-rank test. Cox proportional hazard model was used to assess independent association of CKD with long-term survival after adjusting for potential confounders.

Results: A total of 1206 patients were included. Of these 544 had normal renal function, 454 moderate CKD, and 208 severe CKD. Patients with CKD as compared to normal renal function, were more likely to be female and had greater prevalence of comorbidity including hypertension, coronary artery disease, and heart failure. Over a median follow up of 4.2 years (IQR 2.9-6.5), patients with CKD had lower survival rates (p<0.001) (Figure). After adjusting for baseline co-morbidities, moderate CKD (HR 1.6, 95% CI 1.2-2.1) and severe CKD (HR 4.4; 95% CI 3.2-5.9) were independent predictors of mortality.

Conclusion: CKD is a powerful and independent predictor of long-term mortality in patients with persistent AF undergoing elective electrical cardioversion. Further studies evaluating mediators of this association are needed.

P2476 | BEDSIDE
Mortality in valvar and non-valvar atrial fibrillation: insights from a nationwide cohort analysis - TRAF (Turkish AF database)
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Background: Atrial fibrillation (AF), the most common clinical arrhythmia, has a valvar or non-valvar etiology and causes significant morbidity and mortality. However, there is no robust data about the occurrence and the predictors of mortality in patients with valvar AF. Our objective was to compare the predictors of all-cause mortality in valvar and non-valvar AF patients in a large cohort.

Methods: We analyzed the records of 542,130 patients over the age 18 who had the diagnosis of valvar and non-valvar AF according to ICD-10 code I48 from
Conclusions: Although the exact mechanism has not been highlighted, patients with non-valvular AF had worse long-term prognosis compared to valvular AF patients. Age and heart failure were found as the most important common prognostic factors in prediction of all-cause mortality in these group of patients.

### P2477 | BEDSIDE

Electrophysiological implications on the thinning of left atrial wall; complex fractionated electrogram, voltage and cycle length


**Purpose:** Atrial scars are strongly related to slow anisotropic conduction. Their relationship to atrial thickness has not yet been investigated. This study sought to evaluate the relationship between left atrial wall thickness (LAWT) imaged by multidetector computer tomography (MDCT) and arrhythmia substrate in atrial fibrillation (AF).

**Methods:** Atrial MDCT of 20 patients with AF (12 persistent AF) was registered with electroanatomic map to measure the complex fractionated electrogram, voltage and cycle length (CFL). Local mean cycle length (MCL) and voltage (LV) of LA were analyzed with regard to LAWT.

**Results:** There were large variations in LAWT (median: 1.77 mm, range 0.77–4.17 mm), LA voltage (median: 0.15 mV, range 0.02–6.01 mV) and local MCL (median: 180.87 ms, range 51.33–257.67 ms). LAAA base had the thickest wall (2.27±0.51mm), the highest voltage (1.26±1.37 mV) and the shortest MCL (166.64±0.43mm). Post-operative contrast performed 1 month after showed the thickest wall (1.66±0.43mm) and the lowest voltage (0.43±0.02 mV), and the floor of LA showed the longest MCL (384.41±177.80 ms). LAWT was thinner in areas with- out than in those with complex fractionated electrogram (1.71±0.42 vs 2.38±0.65 mm, p<0.01). Finally, LAWT was significantly thicker in area (n=206) with low voltage (<0.1 mV) than those (n=333) with high voltage (≥0.1 mV) (1.82±0.55 vs. 1.93±0.58 mm, p=0.04).

**Conclusions:** Thin LAWT was associated with low LA voltage, long local MCL and less complex fractionated electrogram. These findings suggest that the structural remodeling is related with functional change of atrial substrate in patients with AF.

### P2478 | SPOTLIGHT

Feasibility and effectiveness of structured hospital based nurse-led atrial fibrillation service

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**Purpose:** Incidence and predictors of post-operative new onset atrial fibrillation in rheumatic heart disease patients undergoing valve surgery

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**Purpose:** The relative risk of stroke in rheumatic heart disease (RHD) patients with Atrial Fibrillation (AF) is 17-fold. There is paucity of studies focusing on the outcomes of de novo AF after valve surgery for RHD. The current study was designed to look for the incidence and predictors of new onset AF in RHD undergoing valve surgery.

**Methods:** Postoperative patients who had undergone valve surgery for RHD during the previous 5 years and who were in NSR preoperatively were recruited from the outdoor patient department. Their rhythm status at follow up was assessed by electrocardiogram (ECG) recordings. Pre-operative demographic profile and valve hemodynamics on echocardiography were analyzed.

**Results:** Of the 405 patients (male=250, female=155) studied, 39 patients (9.63%) developed AF at a follow-up of 5 years (mean 2.65±1.3 years). At surgery, the mean age of patients in normal sinus rhythm (NSR) was 29.41±7.88 years, 61% men, 62% paroxysmal AF. Mean CHA2DS2VASc score was 2.4 (0; 7), mean HASBLED score 0.8 (0; 3). Number of visits was 1.9 (1; 7). At first visit 98% of patients with a CHADS2VASc score ≥1 were on OAC (62% warfarin, 38% NOAC). Of patients with a CHADS2VASc score ≥2 were 99% on OAC (61% warfarin, 39% NOAC). During 449 (0; 1.9) years of follow-up we observed 1 TIA, 0 stroke, 4 major bleeds and 6 deaths of which 1 was cardiovascular, 4 cancer-related, and 1 unclassified.

**Conclusions:** Compared to published data on use of OAC and prognosis in AF, our early results of structured nurse-led AF service suggest great promise for the future. Further evidence and long time follow-up data are warranted.

### P2479 | BEDSIDE

A prospective study of supraventricular activity and incidence of atrial fibrillation

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**Purpose:** Atrial fibrillation (AF) is thought to be caused by an electrical trigger reaching a susceptible atria. Such a trigger could be present long before the occurrence of arrhythmia. We sought to determine if supraventricular extrasystoles (SVES) and supraventricular tachycardias (SVT) measured at 24 h Holter ECG were associated with increased incidence of AF.

**Methods:** In 1988–1991, 438 individuals (44% men, mean age 65 years were examined using 24 h Holter ECG. Six individuals with prevalent AF were excluded. After a mean follow-up of 10.3 years there were 45 cases of incident AF. Hazard ratios (HR) were computed using multivariable Cox regression modelling adjusting for age, gender, systolic blood pressure and HOMA-IR.

**Results:** Frequency of SVES as well as SVT episodes per 24 h were independent predictors of incident AF, HR 1.26, 95% confidence interval (CI) 1.07–1.49, p<0.0006; and HR 1.35, 95% CI 1.10–1.65, p=0.004 respectively. Further adjustment for smoking, education, alcohol and use of medication and physical activity did not substantially alter results, nor did analysis using competing risks regression accounting for a competing risk of death. Incidence of AF was substantially increased especially in individuals with SVES in the top quintile of the distribution.

**Conclusion:** SVES and SVT independently predict AF.

### P2480 | BEDSIDE

Incidence and predictors of post-operative new-onset atrial fibrillation in rheumatic heart disease patients undergoing valve surgery

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**Purpose:** The relative risk of stroke in rheumatic heart disease (RHD) patients with Atrial Fibrillation (AF) is 17-fold. There is paucity of studies focusing on the outcomes of de novo AF after valve surgery for RHD. The current study was designed to look for the incidence and predictors of new onset AF in RHD undergoing valve surgery.

**Methods:** Postoperative patients who had undergone valve surgery for RHD during the previous 5 years and who were in NSR preoperatively were recruited from the outdoor patient department. Their rhythm status at follow up was assessed by electrocardiogram (ECG) recordings. Pre-operative demographic profile and valve hemodynamics on echocardiography were analyzed.

**Results:** Of the 405 patients (male=250, female=155) studied, 39 patients (9.63%) developed AF at a follow-up of 5 years (mean 2.65±1.3 years). At surgery, the mean age of patients in normal sinus rhythm (NSR) was 29.41±7.88 years, 61% men, 62% paroxysmal AF. Mean CHA2DS2VASc score was 2.4 (0; 7), mean HASBLED score 0.8 (0; 3). Number of visits was 1.9 (1; 7). At first visit 98% of patients with a CHADS2VASc score ≥1 were on OAC (62% warfarin, 38% NOAC). Of patients with a CHADS2VASc score ≥2 were 99% on OAC (61% warfarin, 39% NOAC). During 449 (0; 1.9) years of follow-up we observed 1 TIA, 0 stroke, 4 major bleeds and 6 deaths of which 1 was cardiovascular, 4 cancer-related, and 1 unclassified.

**Conclusions:** Compared to published data on use of OAC and prognosis in AF, our early results of structured nurse-led AF service suggest great promise for the future. Further evidence and long time follow-up data are warranted.
B). The biomarker score provided greater discrimination than CHA2DS2-VASc

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Background: Treatment decisions in atrial fibrillation (AF) are based on clinical assessment of the risk of stroke, systemic embolism (SEE), or death. The CHA2DS2-VASc risk score is pragmatic and widely used but has moderate discrimination. We investigated the performance of multiple cardiovascular biomarkers alone and in combination as a biomarker score for risk prediction in patients with AF.

Methods: We measured cardiac troponin (cTnl), NTproBNP, and D-dimer in baseline at 4880 subjects enrolled in the biomarker substudy of the ENGAGE-AF trial of the FXa inhibitor edoxaban vs. warfarin. All endpoints were adjudicated by a central events committee. Median follow-up was 2.8 years.

Results: Each of the biomarkers examined was associated with a graded risk of stroke/SEE/death after adjustment for the CHA2DS2-VASc score (global p < 0.0001, Panel A). NTproBNP, cTnl, and D-dimer each identified a > 2.5-fold gradient of risk across groups of increasing concentration. A multimarker risk score was developed, assigning tiered points for higher concentrations (Panel B). The biomarker score provided greater discrimination than CHA2DS2-VASc (Panel B) and when combined with CHA2DS2-VASc improved the c-statistic to 0.71 (p < 0.004 vs. markers alone; p < 0.0001 vs. CHA2DS2-VASc alone).

Conclusion: A multimarker risk score appears to significantly enhance the assessment of risk compared with traditional clinical risk stratification alone for stroke/SEE/death in patients with AF. Incorporation of biomarkers into clinical decision-making for anticoagulation in AF warrants consideration.

P2482 | BEDSIDE

Clinical characteristics and one-year outcomes of atrial fibrillation patients under rate- or rhythm-control strategy: From the Fushimi AF Registry

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Purpose: Atrial fibrillation (AF) increases the risks of stroke, congestive heart failure (CHF) and mortality, and the prevalence of AF is increasing significantly (reportedly, 0.6% of total population in Japan). There are two major treatment strategies for AF: rate-control and rhythm-control. Recent clinical trials in patients with AF have shown that a rate-control strategy was non-inferior in preventing clinical events, compared with a rhythm-control strategy.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients in Fushimi-ku, Kyoto, Japan. Fushimi-ku is densely populated with a total population of 283,000, and is assumed to represent a typical urban community in Japan. At present, we have enrolled 3,821 patients (1.4% of total population) from March 2011 to December 2013. One-year follow-up was completed in 2,985 patients as of December 2013. We aimed to investigate differences in baseline clinical characteristics and one-year outcomes between AF patients under rate-control strategy (n=1,089, 37%), rhythm-control strategy (n=570, 19%), and neither of them (n=1,306, 44%).

Results: The mean age was lower in rhythm-control group than rate-control or neither group (rate, rhythm, neither: 74.0±10.4, 71.7±10.8, 74.7±10.1 years; p < 0.01). Rate-control group was lower in systolic blood pressure (121.9±18.2, 125.5±18.4, 126.3±19.6 mmHg; p < 0.01), had higher prevalence of CHF (39.1%, 13.9%, 22.5%; p < 0.01), higher prevalence of coronary artery disease (19.2%, 11.0%, 13.6%; p < 0.01), received more oral anticoagulants (66.1%, 50.5%, 42.8%; p < 0.01) and more antiplatelet agents (33.5%, 28.2%, 28.7%; p < 0.02). Rhythm-control group was lower in resting heart rate (78.3±15.5, 74.3±14.3, 78.1±13.2 bpm; p < 0.01), had lower CHADS2 score (5.2±1.2, 7.1±1.25, 2.11±1.39; p < 0.01), fewer previous stroke (18.2%, 14.4%, 22.4%; p < 0.01), and were more asymptomatic (47.1%, 73.7%, 40.3%; p < 0.01). One-year mortality was significantly lower in rhythm-control group (8.5%, 3.9%, 9.6%; p < 0.01), and the incidence of CHF hospitalization was significantly higher in the rate-control group (6.2%, 1.8%, 3.3%; p < 0.01). The incidence of stroke was not significantly different between the three groups (2.6%, 1.9%, 2.8%; p = 0.5).

Conclusion: The Fushimi AF registry represents the clinical profile of real-world Japanese AF patients. Rate-control and rhythm-control are two different treatment strategies of AF patients. The two strategies were selected depending on the clinical background such as age, symptom, and various comorbidities, and this affected the one-year clinical outcomes.

P2483 | BENCH

Cognitive and psychosomatic impairments in patients with different forms of atrial fibrillation

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Aims: To determine the features of cognitive and psychosomatic impairments in patients with different forms of atrial fibrillation (AF) using sensitive diagnostic techniques.

Materials and methods: We examined 81 patients (33 women and 48 men, aged 62.6±15.6 years, 23 people with persistent form of AF, 28 patients with paroxysmal AF, in 14 cases - permanent AF. AF cases were such disease as: hypertension in 45 patients (55.5%), ischemic heart disease in 23 patients (28.4%), myocardial infarction in 5 patients (6.2%), mitral valve disease detected 1 person (1.2%), idiopathic AF in 7 patients (8.6%). Comparison group of persons without AF matched by sex and age and the underlying pathology was examined. We evaluated the cognitive function of participants using the program “Status PF”. Visual memory, attention span, vision field, cognitive abilities (simple analogy, linguistic thinking), neuromodynamics (simple visual-motor response, complex visual-motor reaction, the reaction to a moving object). A daily monitoring of ECG was used for registration subclinical forms of atrial fibrillation.

Results: We found that decline visual memory occurred in all patients with AF. They reproduced 3.8±1.5 numbers and 4.5±1.5 words, whereas in the comparison group were comparable: 14.6±1.5 numbers and 6.6±1.4 words (p < 0.01). Attention was declined almost twice. For example, founding of numbers in the test “vision field” by patients with AF took 32±9±14.6 seconds and in the comparison group 18.4±2.6 seconds (p < 0.01). Mild impairment mind abilities were identified. Patients earned 8±2.7 points in the test “Symbolic Mind”, versus 10±2.0 points (p < 0.01) and the test “Linguistic Thinking (abstract)” - 3.8±1±2.9, versus 4.9±2.0 points (p < 0.01). One-year mortality was 13.9%, 22.5%; p < 0.01), had higher prevalence of CHF (39.1%, 13.9%, 22.5%; p < 0.01), received more oral anticoagulants (66.1%, 50.5%, 42.8%; p < 0.01) and more antiplatelet agents (33.5%, 28.2%, 28.7%; p < 0.02). Rhythm-control group was lower in resting heart rate (78.3±15.5, 74.3±14.3, 78.1±13.2 bpm; p < 0.01), had lower CHADS2 score (5.2±1.2, 7.1±1.25, 2.11±1.39; p < 0.01), fewer previous stroke (18.2%, 14.4%, 22.4%; p < 0.01), and were more asymptomatic (47.1%, 73.7%, 40.3%; p < 0.01). One-year mortality was significantly lower in rhythm-control group (8.5%, 3.9%, 9.6%; p < 0.01), and the incidence of CHF hospitalization was significantly higher in the rate-control group (6.2%, 1.8%, 3.3%; p < 0.01). The incidence of stroke was not significantly different between the three groups (2.6%, 1.9%, 2.8%; p = 0.5).

Conclusion: The Fushimi AF registry represents the clinical profile of real-world Japanese AF patients. Rate-control and rhythm-control are two different treatment strategies of AF patients. The two strategies were selected depending on the clinical background such as age, symptom, and various comorbidities, and this affected the one-year clinical outcomes.

P2484 | BEDSIDE

Baseline characteristics and clinical outcomes of patients with atrial fibrillation undergoing catheter ablation: from the Fushimi AF registry

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Background: Catheter ablation (CA) has become an effective treatment for atrial fibrillation (AF), yet it is not well established as a first-line intervention for the AF management, with limited cohort investigations including clinical outcome data.

Methods: The Fushimi AF Registry, a community-based prospective survey, was...
Radiofrequency Ablation (RFA) for Atrial Fibrillation (AF) is a well-established treatment modality when medical therapy fails. Patients with diminishing LVEF after proper management of AF are retrospectively labeled as having Tachycardia Induced Myopathy (TIM). However, predictors of recovery at the time of the ablation have not been well defined in the literature.

**Purpose:** We aim to fill this gap by providing a predictor model for LVEF improvement after AF RFA.

**Methods:** Prospectively collected data on 37 relevant clinical variables of 153 consecutive patients with AF and decreased LVEF (<50%) that underwent RFA at a tertiary care center were analyzed. Two groups were identified: a group that fully recovered LVEF to an absolute value of >50%, and those that did not recover to that extent. Relevant clinical variables of the two groups were compared by univariable analysis. Variables that were statistically significant at a 0.1 significance level were entered in a stepwise logistic regression analysis and kept in the final model if they were significant at the 0.05 significance level. The final multivariable logistic prediction model of LVEF recovery was assessed for goodness of fit and discriminatory power.

**Results:** Univariable analysis showed that being female (p: 0.015), presenting with higher pre-RFA ejection fraction (p: 0.003), absence of Implantable Cardioverter Defibrillator (ICD) (p: 0.046), previous AF RFA (p: 0.019), shorter duration of the QRS (p: 0.031) and paroxysmal as compared to persistent AF (p: 0.05) were positive predictors of LVEF recovery above 50%. Age, left atrium diameter, history of coronary artery disease, rhythm and heart rate among others were not found to be associated with LVEF recovery in this cohort. The final model included baseline ejection fraction, gender, ICD and number of previous ablations (Homes Lemeshow p: 0.9093 and area under ROC: 0.7114).

**Conclusions:** The 4 variables that were kept in the final model may be used to identify subgroups of patients that were likely to recover LVEF after AF RFA, provide personalized advice to patients, and serve as a guide for future research. In the future, we will validate this model in another cohort of patients.

**Clinical outcomes in atrial fibrillation III**

**P2486 | BEDSIDE**

**Risk of acute myocardial infarction in patients with atrial fibrillation having a CHA2DS2-VASC score of 0 or 1**

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**Background:** The risk of acute myocardial infarction (AMI) in patients with atrial fibrillation (AF) having a CHA2DS2-VASC score of 0 (for males) or 1 (for females) has not been investigated before. The goal of the present study was to compare the risk of AMI between AF and non-AF subjects with a low CHA2DS2-VASC score.

**Methods:** This study used the “National Health Insurance Research Database” in Taiwan. A total of 7,254 AF males (CHA2DS2-VASC score = 0) and 4,860 AF females (CHA2DS2-VASC score = 1) without receiving antithrombotic therapies were selected as the study group. For each study patient, one age-, sex-, and CHA2DS2-VASC score matched subject without AF were randomly selected to constitute the control group (n=12,114). The clinical endpoint was the occurrence of AMI.

**Results:** During the follow up of 5.7±3.6 years, 258 patients (1.1%) suffered from AMI with an annual incidence of 0.29% and 0.10% for AF and non-AF patients, respectively. AF was a significant risk factor of AMI with a hazard ratio (HR) of 2.927 (95% confidence interval [CI] = 2.214-3.869, p<0.001) after the adjustment for potential confounders. The Kaplan-Meier curve of freedom from AMI is shown in Figure 1. Although the AF increased the risk of AMI in AF females (HR = 4.215) more substantially than in males (HR = 2.720) compared to non-AF patients, the risk of AMI was higher in AF males than that of non-responders with an adjusted HR of 2.235 (95% CI = 1.608-3.106, p<0.001).

**Conclusions:** In patients with a CHA2DS2-VASC score of 0 or 1, AF was an important risk factor of AMI.

**P2487 | BEDSIDE**

**Predicators of left ventricular function improvement after radiofrequency ablation in a large cohort of patients referred for atrial fibrillation ablation**

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**Introduction:** Radiofrequency Ablation (RFA) for Atrial Fibrillation (AF) is a well-established treatment modality when medical therapy fails. Patients with diminishing LVEF at the time of the ablation and at baseline that did not recover after proper management of AF are retrospectively labeled as having Tachycardia Induced Myopathy (TIM). However, predictors of recovery at the time of the ablation have not been well defined in the literature.

Purpose: To fill this gap by providing a predictor model for LVEF improvement after AF RFA.

Methods: We aim to fill this gap by providing a predictor model for LVEF improvement after AF RFA. Prospectively collected data on 37 relevant clinical variables of 153 consecutive patients with AF and decreased LVEF (<50%) that underwent RFA at a tertiary care center were analyzed. Two groups were identified: a group that fully recovered LVEF to an absolute value of >50%, and those that did not recover to that extent. Relevant clinical variables of the two groups were compared by univariable analysis. Variables that were statistically significant at a 0.1 significance level were entered in a stepwise logistic regression analysis and kept in the final model if they were significant at the 0.05 significance level. The final multivariable logistic prediction model of LVEF recovery was assessed for goodness of fit and discriminatory power.

Results: Univariable analysis showed that being female (p: 0.015), presenting with higher pre-RFA ejection fraction (p: 0.003), absence of Implantable Cardioverter Defibrillator (ICD) (p: 0.046), previous AF RFA (p: 0.019), shorter duration of the QRS (p: 0.031) and paroxysmal as compared to persistent AF (p: 0.05) were positive predictors of LVEF recovery above 50%. Age, left atrium diameter, history of coronary artery disease, rhythm and heart rate among others were not found to be associated with LVEF recovery in this cohort. The final model included baseline ejection fraction, gender, ICD and number of previous ablations (Homes Lemeshow p: 0.9093 and area under ROC: 0.7114).

Conclusions: The 4 variables that were kept in the final model may be used to identify subgroups of patients that were likely to recover LVEF after AF RFA, provide personalized advice to patients, and serve as a guide for future research. In the future, we will validate this model in another cohort of patients.
ECG monitoring between 3 and 12 months after ablation, AF recurrences > 30 sec were observed in 113 patients (35%). While the CHADS2 (AUC 0.577, 95% CI 0.505-0.650, p=0.037) and CHADS2-VASc scores (AUC 0.590, 95% CI 0.518-0.663, p=0.015) demonstrated low predictive value, the APPLE score ranging from 0 to 5 points, showed better prediction of AF recurrences (AUC 0.617, 95% CI 0.548-0.680, p<0.002). Patients with APPLE score of 0 (20% of cohort), 1 (32%), 2 (23%), and ≥3 (8%) had AF recurrence rates of 18%, 38%, 39%, and 56%, respectively (p=0.001). Compared to patients with an APPLE score of 0, the risk (OR) for AF recurrences was 2.9 (95% CI 1.4-6.3, p=0.006), 3.0 (95% CI 1.3-6.6, p=0.032) and 6.0 (95% CI 2.2-16.8, p=0.001) for APPLE scores 1, 2, or ≥3, respectively.

**Conclusion:** The novel APPLE score is superior to the CHADS2 and CHA2DS2-VASc scores for prediction of rhythm outcomes after repeat AF catheter ablation and may be a suitable prognostic tool to identify patients with low, intermediate or high risk for AF recurrences.

**P2490 | BEDSIDE**

Predictors of long term outcome of single catheter ablation of atrial fibrillation in patients with ischemic and non-ischemic cardiomyopathies


**Heart Centre, Department of Electrophysiology, Leipzig, Germany**

**Background:** Atrial fibrillation (AF) frequently coexists with cardiomyopathies and is associated with worsened cardiovascular outcome, aggravated heart failure symptoms and frequent ventricular arrhythmia. In that context, catheter ablation which has been proved to reduce AF burden and improve left ventricular function can ameliorate those adverse effects but the identification of suitable patients is crucial. Therefore, this study aimed to evaluate predictors of long term success of AF ablation in cardiomyopathy patients.

**Methods:** In 73 consecutive patients (mean age 59±10 years, 85% male, mean EF 37±12%) with ischemic (n=30) or dilated cardiomyopathy (n=43) undergoing AF catheter ablation, the predictors of long term outcome were analysed by Cox proportional hazards model. AF recurrence was monitored with 7-day Holter ECG after 6 and 12 months after ablation.

**Results:** During mean follow-up of 14±10 months, AF recurrence was observed in 32 patients (44%). The median freedom from AF was 11 months after 6 and 12 months after ablation.

**Conclusions:** Diabetes mellitus, left atrial dimension, and left ventricular dimension are associated with late AF recurrence after catheter ablation.

**P2491 | BEDSIDE**

Randomized comparison of continuous and intermittent heparin infusion during catheter ablation of atrial fibrillation; COHERE (Continuous Heparin infusion REIrrigation to ablation of atrial fibrillation)


**Background:** We hypothesized that continuous heparin infusion would be favorable for maintenance of heparin concentration during catheter ablation of atrial fibrillation (AF).

**Methods:** One hundred forty two patients undergoing AF ablation were consecutively enrolled and randomized to intermittent or continuous heparin infusion. A dose of heparin was determined to maintain optimal activated clotting time (ACT) 392±184 sec, which were checked every 30 minute during procedure. The primary endpoint was the frequency of the maintenance of optimal ACT.

**Results:** There was no significant difference of age (years, 61±10 vs. 60±12, P=0.89), sex (male, 45/71 vs. 52/71, P=0.5), body surface area (m2, 1.73±0.20 vs. 1.78±0.20, P=0.14) and baseline INR (1.86±0.58 vs. 1.84±0.48, P=0.82) between intermittent and continuous group. In intermittent group, the frequency of optimal ACT was only about 55%. After learning curve, the frequency of optimal ACT was raised up to about 70% with lower dose of total heparin in continuous group (Table).

**Conclusions:** During catheter ablation of AF, continuous heparin infusion was useful to maintain optimal ACT range with lower dose of heparin and small ACT fluctuations.

**P2492 | BEDSIDE**

N-acetyl cysteine for the prevention of early recurrence after radiofrequency catheter ablation in patients with persistent atrial fibrillation: a randomized, double-blind, placebo-controlled study

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**Introduction:** Early recurrence (ER) after radiofrequency catheter ablation (RFCA) in patients with atrial fibrillation (AF) is associated with endothelial dysfunction caused by iatrogenic myocardial injury. Although N-acetylcysteine (NAC) may effectively reduce the incidence of post-operative AF, there was no data regarding effect of NAC on prevention of ER after AF ablation.

**Methods:** We randomly assigned 100 consecutive patients with persistent AF to NAC (n=50) or placebo (n=50) group. NAC was intravenously infused for 1 hr before RFCA at a dose of 50 mg/kg, followed by continuous infusion for 48 hr after RFCA at a dose of 50 mg/kg/day. Immediately before and after RFCA, index of microvascular resistance (IMR) was assessed at left anterior descending coronary artery and blood samples were obtained from coronary sinus for analysis of nitric oxide (NO) and activated leukocyte cell adhesion molecule (ALCAM).

**Results:** There were no significant differences between 2 groups in baseline demographics, CHADS2 score, and left atrial volume (LAV). IMR and ALCAM was increased, and NO was decreased after RFCA. Compared with placebo group, changes in IMR and NO were significantly diminished in NAC group. During follow-up period of 3 months, AF recurred 19 patients in placebo group and 7 patients in NAC group (P=0.007). In multivariate logistic analysis, NAC administration, LAV, and change in IMR were independently related to ER.

**Conclusions:** NAC administration was significantly reduced ER after RFCA in patients with persistent AF. These might attribute to prevent the deterioration of endothelial function caused by iatrogenic myocardial damage.

**P2493 | BEDSIDE**

Incidence and clinical characteristics of transient ST-T elevation during transseptal catheterization for atrial fibrillation Ablation


**Background:** Transient ST-T elevation is a rare complication during transseptal catheterization. This study aimed to delineate the incidence, characteristics of transient ST-T elevation during transseptal catheterization for atrial fibrillation (AF) ablation.

**Methods:** From January 2006 to January 2013, consecutive patients underwent transseptal catheterization for circumferential pulmonary vein radiofrequency ablation in our hospital were enrolled prospectively. Breakthrough transseptal catheterization was performed guided by fluoroscopy.

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**Table:**

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<tr>
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<td>(n=71)</td>
<td>(n=71)</td>
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<tr>
<td>Total dose of heparin (u)</td>
<td>12873±392</td>
<td>12896±3755</td>
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<tr>
<td>Heparin infusion time (hr)</td>
<td>2.4±0.5</td>
<td>2.4±0.6</td>
<td>0.91</td>
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<tr>
<td>Average of ACT (sec)</td>
<td>363±39</td>
<td>330±37</td>
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<tr>
<td>Standard deviation of ACT (sec)</td>
<td>64±34</td>
<td>43±18</td>
<td>0.01</td>
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<tr>
<td>The frequency within optimal ACT (300–400 sec)</td>
<td>771±43 (53.8%)</td>
<td>79±144 (84.9%)</td>
<td>0.95</td>
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**Figure 1:**
Results: Out of the 3452 patients, 13 patients (0.38%) (mean age 57±8.6 years, 6 females, 12 paroxysmal AF, mean left atrial diameter 35.4±3.8 mm) had ST elevation without sequelae. Catheter ablation of AF could be safely completed in these patients. No symptoms. Coronary artery angiography was performed in one patient with chest pain, one patient complained of dizziness, and one patient had normal saline iv drip. Catheter ablation of AF was completed in all the patients without sequelae and other complications. Four of the 13 patients (30.8%) had recurrence after a mean 21.7-month follow-up.

Conclusion: ST-T elevation was a rare complication of transseptal catheterization without sequelae. Catheter ablation of AF could be safely completed in these patients.

P2494 | SPOTLIGHT
Presence and extent of coronary artery disease as predictor for AF reoccurrence after catheter ablation: The Leipzig Heart Center AF Ablation Registry
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Background: Previous studies have suggested that occlusion of the right coronary artery (RCA) promotes atrial fibrillation (AF) by creating a right atrial substrate. However, the presence and extent of coronary artery disease (CAD) is usually not considered to tailor AF ablation strategies. In particular, right atrial ablation is not routinely being performed in patients with RCA disease. Therefore, we analyzed the possible association between the presence and extent of CAD and rhythm outcomes of left-atrial AF catheter ablation.

Methods and results: 1310 patients (60±10 years, 67% males, 63% paroxysmal AF) from the Leipzig Heart Center AF Ablation Registry undergoing de novo AF catheter ablation were included. Of those, 152 patients (11.6%) had significant CAD (stenosis >50%); 89 (59%) had one, 35 (23%) two and 28 (18%) three vessels diseased. CAD was associated with a median of 72 (IQR 3-219) AF recurrences. Asymptomatic CAD was associated with an increased AF recurrences compared with patients without CAD (p<0.001). Coronary angiography was performed in one patient with negative finding. All the patients recovered in 4.2 mins (2-10 mins) with dopamine or fast saline iv drip. Catheter ablation of AF was completed in all the patients without sequelae and other complications. Four of the 13 patients (30.8%) had recurrence after a mean 21.7-month follow-up.

Conclusion: The presence and extent of CAD does not impact on rhythm outcome of AF catheter ablation in the entire cohort. However, individualized AF ablation strategies need to be assessed to improve overall outcomes.

P2495 | BEDSIDE
NT-proBNP as a marker for silent AF
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Background: Atrial fibrillation (AF) is a common cause of ischaemic stroke. This risk can be ameliorated using oral anticoagulant (OAC) therapy. Screening for atrial fibrillation (AF) using pulse palpation is recommended above the age of 65 according to the European Society of Cardiology. AF detection remains difficult when asymptomatic. NT-proBNP is an established cardiac biomarker, indicating congestive heart failure and can be used as a predictor for stroke risk in patients with AF, especially if used in addition to CHA2DS2-VASC risk stratification score. An increased NT-proBNP is associated with development of AF.

Methods: The STROKESTOP study is a mass-screening study using intermittent ECG recordings for detection of undiagnosed atrial fibrillation (AF) comprising 6 888 screened individuals. Preliminary results show that 3% of the screened population were not known AF, and furthermore that 2% of the participants had known AF, that was not treated with OAC. In a substudy to the STROKESTOP study 89 patients with undiagnosed AF and 500 patients without detected AF had blood samples drawn for NT-proBNP analysis.

Results: Individuals with newly diagnosed AF (n=89) had a NT-proBNP mean of 555±SD 683, vs those in sinus rhythm (n=500) mean 268±SD 408 (p=0.011). Clinical characteristics did not differ between the groups.

Conclusion: A significantly increased NT-proBNP was found in individuals with silent AF as compared to individuals without AF. NT-proBNP can be used as a marker for undiagnosed silent AF.

P2497 | BENCH
Inhibition of DPP-4 restores myocardial autophagic flux and reduces mortality after myocardial infarction in diabetic rats
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Purpose: The mechanism by which diabetes increases mortality after myocardial infarction (MI) remains unclear. In this study, we examined the hypothesis that disturbed autophagic processes are involved in aggravation of heart failure after myocardial infarction (MI) by type 2 diabetes mellitus (T2DM), which is treatable by a dipeptidyl peptidase-4 (DPP-4) inhibitor.

Methods and results: Body weight (625±5 g vs 523±3 g), fasting plasma glucose (FPG: 288±41 vs. 135±5 mg/dl) and glycoalbumin (15.3±2.0 vs. 10.1±0.7%) were significantly higher in OLETF, a rat model of obese T2DM, than in LETO, a nonobese control (both 25-30 weeks of age). Treatment with vildagliptin (10 mg/kg/day), a DPP-4 inhibitor, for 2 weeks did not significantly affect body weight, FPG or glycoalbumin level in OLETF. Under baseline conditions after a 12-hr fast, levels of phospho-Akt, -mTOR and -p70S6 kinase in the myocardium...
were lower and phospho-AMP kinase and -ULK-1 were higher in OLET than in LETO, indicating pro-autophagic signalling in OLET. LC3-II level was higher in OLET than in LETO, though p62 protein levels were comparable. The mRNA levels of LAMP2, Rab7, and cathepsins were similar in LETO and OLET. At 12 hrs after MI by ligation of the left coronary artery, LC3-II protein in the non-infarcted remote myocardium increased in LETO. In OLET, however, LC3-II protein was decreased and p62 protein accumulated in the non-infarcted remote myocardium after MI, indicating disruption of autophagic clearance. Treatment with vildagliptin increased LC3-II level and reduced p62 protein after MI in OLET, indicating restoration of autophagic flux. The effects of vildagliptin on autophagic flux were mimicked by exenatide (10 mg/kg/day), a GLP-1 receptor agonist. Mortality at 48 hrs after MI in OLET (70%) was significantly higher than that in LETO (19%). Vildagliptin did not affect post-MI mortality in LETO (17%) but significantly reduced mortality in OLET (20%). The mitigation of mortality in OLET by vildagliptin was mimicked by exenatide (37%) and was abrogated by chloroquine (10 mg/kg/day), an inhibitor of autophagy (67%), administered for 7 days before MI.

Conclusion: The findings suggest that disturbed autophagic clearance in the non-infarcted myocardium contributes to increased severity of heart failure by T2DM. Inhibition of DPP-4 reduces post-MI mortality presumably by restoration of autophagic processes in the non-infarcted region of the diabetic myocardium.

P2499 | BENCH Carbon monoxide releasing molecule alters microRNA expression and improves structural and functional cardiac recovery after myocardial infarction

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Purpose: Carbon monoxide (CO), produced by heme oxygenase-1 (HO-1) from heme, is an endogenous paracrine factor involved in the regulation of blood pressure and vasodilatory structure and function. The mechanisms behind the cardioprotective properties of CO are still poorly understood. We studied the effects of a synthetic CO-releasing molecule (CORM-3) on cardiac remodelling and repair after myocardial infarction as well as on expression of microRNAs (miRNAs), novel molecules regulating gene function.

Methods: Male Wistar rats with myocardial infarction (MI), induced by coronary ligation (n=75), or sham-operated controls (n=75) were treated from day 4 to day 14 after MI either with synthetic CORM-3 (20 mg/kg i.p.) or with inactive iCORM and sacrificed at 2, 4 or 8 weeks after MI. Infarct size, amount of cardiomyocytes, and vascular and capillary densities in the infarct and border areas were determined. Ki67 staining was used to quantify proliferative cells and c-kit staining to determine stem/progenitor cells. Cardiovascular disease miScript miRNA PCR Array was used for miRNA profiling and real-time RT-PCR for quantification of individual miRNAs. Western blotting was utilized to evaluate protein expression and exochordiography to assess cardiac structure and function.

Results: Treatment with CORM-3 enhanced recovery of MI compared with iCORM. CORM-3 increased the proportion of cardiomyocytes (p<0.05 vs. CORM-3) and capillary and vascular densities (p<0.05 vs. iCORM) in the infarct area. Ejection fraction improved (p<0.05) and left ventricular volumes decreased (p<0.05) in CORM-3 treated MI groups compared to iCORM treated rats with MI. The amount of Ki67+ cardiomyocytes or c-kit+ progenitor cells did not differ between CORM-3 and iCORM MI groups. Compared to iCORM treated rats, CORM-3 treatment increased protein expression of angiogenic factors VEGF-B, HIF-1α, HGF and PDI, and up-regulated the expression of several miRNAs (including miR-133a and miR-208a) which were down-regulated at weeks 2 and 4 after MI.

Conclusions: The synthetic CO releasing molecule CORM-3 improved both structural and functional cardiac recovery after myocardial infarction. These effects were associated with increased expression of angiogenic factors and altered expression of several miRNAs involved in myocardial homeostasis, remodelling, and repair. Modulation of HO-1-COX axis and selected miRNAs may prove novel drug targets to facilitate cardiac recovery after myocardial infarction.

P2500 | BENCH Optimizing the cardioprotective effects of remote ischemic preconditioning

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Purpose: Remote ischemic preconditioning (rIPC) induced by brief periods of ischemia and reperfusion (IR) to a limb induces protection against cardiac IR injury. The purpose of this study was to determine the duration, of each cycle and quantity of muscle mass determines the efficacy of rIPC for cardioprotection remains unknown. To optimize the efficacy of rIPC-induced cardioprotection, we investigated the impact of each of these potential determinants.

Method: Using male C57BL/6 mice, we compared sham with rIPC treated animals (n=10 in each group). The rIPC protocol consisted of: (A) 2, 4, 6, or 8 cycles; (B) 2, 5 or 10 min duration of ischemia in each cycle and (C) single or two hind-limb occlusions. Each period of ischemia was followed by 5 min of reperfusion. Limb ischemia was induced by using a compressing tourniquet. Following rIPC, hearts were subjected to 25 min of global ischemia and 60 min of reperfusion in an ex-vivo perfusion model. Cardioprotection was evaluated by infarct size and post-ischemic hemodynamic function.

Results: The number of rIPC-cycles increased the efficacy of cardioprotection up to 4 cycles, whereas no further protection was seen with 6 and 8 cycles. The amount of muscle mass (number of limbs) had no influence on the efficacy of protection. Cycles of 2 min ischemia offer the same protection as cycles of 5 min, whereas elongated cycles of 10 min ischemia abrogated protection. Post-ischemic hemodynamic function improved in parallel with infarct size.

Conclusions: The number and duration of rIPC cycles, rather than the mass of the effector organ, determine the efficacy of rIPC. rIPC protocols using prolonged periods of ischemia (10 min) do not protect against IR.

P2501 | BENCH Bnip3 is associated with Bax activation during myocardial ischemia/reperfusion-injury in vivo

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Purpose: An acute myocardial infarction (AMI) is associated with cell death of cardiomyocytes via apoptosis and necrosis. The mitochondrial outer membrane permeabilization (MOMP) at the onset of myocardial reperfusion is a major determinant of cardiomyocyte death via apoptosis. MOMP is regulated by pro- and anti-apoptotic Bcl-2 family members. BH3-only proteins, functions as a sensor of stress and transduce these signals to the downstream effectors Bak and Bad, which activation results in the formation of the MOMP, release of apoptogens and finally to caspase activation and cell death. One interesting BH3-only proteins is “Bcl-2 family members BCL2/adenoenovirus E18 19KDa protein-interacting protein 3” (Bnip3). Bnip3 is expressed in adult murine and human hearts. The canonical function of Bnip3 during myocardial ischemia/Reperfusion (I/R) injury is considered to be the trigger of the Bax/Bak pore formation. In an ex vivo I/R model the inhibition of Bnip3 led to a reduction of the infarct size and release of the apoptogens cytochrome C and apoptosis inducing factor (AIF). But the underlying mechanisms are still unidentified.

Methods: Bnip3 is associated with Bax activation during myocardial ischemia/reperfusion-injury in vivo. We found that Bnip3 monomer and dimer are localized in cytosol and mitochondria outer membrane. We could show that Bnip3 interact in vivo with Bax by immuno-precipitation and EPR-spectroscopy. Using the TAT-fusion protein Tat-Bnip3,3.1TM (encoding the carboxyl terminal transmembrane deletion mutant of Bnip3 which act as a dominant negative blocker of Bnip3-induced cell death) we performed an inhibition of Bnip3 and analysed the impact on the infarct size in a murine I/R-Model with 30min of ischemia and 24h of reperfusion. The inhibition of Bnip3 led to a significant reduction of the infarct size (37±7 vs. 18±3% INF/AAR, n=5, p=0.0007) whereas the overexpression using TAT-Bnip3 led to an increase (49±7 vs. INF/AAR, n=9, p=0.048). To show that Bnip3 is involved in Bax activation we analyzed the concentration of active monomer Bax in vivo after 30min ischemia and 5min and 4h reperfusion with and without overexpression of Bnip3 using Western Blot. The overexpression led to earlier activation of Bax. There was an increase of active Bax after 5min whereas under basal condition we found these increase after 4h.

Conclusion: Bnip3 is involved in cell death during myocardial I/R injury by activation of the pore forming factor Bax.
P2502 | BENCH
Postconditioning increases Nrf2 transcriptional activation via PKC pathway and protect hearts against reperfusion injury

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Purpose: Our goal is to provide further information on the endogenous protective mechanisms activated by postconditioning (PostC) in the myocardium, evaluating the activation of the transcription factor Nrf2 by the cardio-protective kinases PKC and PI3K.

Methods and results: Myocardial post-ischemic damage in vivo was produced in male rats by occluding the left anterior descending coronary artery followed by 10 and 60 min of reperfusion (IR group). PostC was applied after arterial occlusion (IR+PostC), followed by 10 and 60 min of reperfusion. Haemodynamic parameters i.e., left ventricular pressure, heart rate, +dP/dt and –dP/dt were maintained in IR+PostC group in compare to IR group. Accordingly, both infarct size and ROS levels were significantly lower in IR+PostC than in the IR group. At such levels, ROS played a role as signaling molecules triggering the intrinsic myocardial protective mechanisms, as we observed an important increase in Nrf2 phosphorylation at Ser40 and Thr/ Tyr residues, which concurred with PKC and PI3K activation. We also observed a higher binding capacity of Nrf2 to the ARE sequence after 60 min of reperfusion and an augmented antioxidant response. Significant increase in both the protein levels and in the enzymatic activity of antioxidant proteins regulated by Nrf2: glutathione S-transferase (GST), copper/zinc-superoxide dismutase (Cu/Zn-SOD) and γ-glutamyl cysteine synthetase (γ-GCS) was observed. To determine the role of cardio-protective kinases in the activation of the Nrf2 pathway, we inhibited PKC or PI3K and evaluated Nrf2 activation, along with the expression of a downstream antioxidant enzyme. Our results indicate that PKC is crucial for Nrf2 activation, since its inhibition with chelerythrine was associated with decreased Nrf2 phosphorylation, lower ARE-binding capacity and diminution in protein levels and enzymatic activities of GST, Cu/Zn-SOD and γ-GCS. Therefore, we propose that the PKC/Nrf2 signaling pathway is part of the endogenous protective mechanisms activated by PostC. On the other hand, we found that PI3K inhibition diminished cardiac performance, although Nrf2 is not target of PI3K, at least not directly.

Conclusions: We propose that the PKC/Nrf2 pathway activation is critical for long-term maintenance of PostC-conferred cardioprotection against reperfusion injury by increasing the antioxidant defense system.

P2503 | BENCH
Cardioprotective and angiogenic effects of miRNAs in human cardiac progenitor cell exosomes

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Background: Exosomes (Exo), actively secreted nanosized membrane vesicles, are being recognized as crucial carriers of intercellular communications. We have shown that Exo from human cardiac progenitor cells (Exo-CPC) significantly reduced cardiomyocyte (CM) apoptosis and stimulated angiogenesis both in vitro and in vivo. We analyzed the miRNA transcrip- tional profile of Exo-CPC compared to exosomes from normal human dermal fibroblasts (Exo-NHDF).

Methods: CPC were derived from atrial explants of patients who underwent heart valve surgery. Exo, precipitated with ExoQuick, were characterized by electron microscopy and FACS analysis. miRNA profiling was analyzed with RT-PCR.

Results: MiRNA323-5p, miRNA132, miRNA133a, miRNA210-3p and miRNA233-5p among the most highly upregulated miRNA in Exo-CPC vs. Exo-NHDF. MiRNA323-5p in Exo-CPC was further upregulated after CPC exposure to hypoxia in vitro. Transfection of pre-miRNA323-5p, pre-miRNA181a, and pre-miRNA132 into HL-1 CM significantly enhanced tolerance to hypoxia/reoxygenation injury (p<0.05 vs. CTRL). Forced miRNA132 overexpression in HUVEC exerted angiogenic effects.

Conclusions: Exo-CPC are cardioprotective both in vitro and in vivo. They are markedly enriched in anti-apoptotic and pro-angiogenic miRNA compared to Exo-NHDF. Hypoxia further increases cytoprotective miRNA in Exo-CPC. Finally, in gain-of-function experiments we identified cardioprotective miRNA against hypoxia/reoxygenation injury.

Figure 1. Exosomes.
Conclusions:
The rats had a large septal artery arising invariably from proximal part of the LCA (n=30) or right coronary artery (n=20). Thirty-three (66%) showed broad MI involving the LAD and LCX territories, and the others (36%) had MI localized to an LAD territory, with intact LCX branching from the septal artery or a short LMT proximally to the LAA (figure). Territory of the septal artery was not sacrificed in any of the anatomical features of the model de novo AHF.

Results:
- In rat hearts subjected to de novo AHF, we also examined the combined effect of metabolic therapy by glucose-insulin (GI) and S1P.
- Metabolic therapy by GI and S1P improved the heart rate (HR) versus controls (148.8 ± 26.4 BPM; p < 0.01 vs. controls; n=6; p < 0.001 vs. S1P+AG490; n=6). STAT3 was increased (p<0.05) in the nuclear fraction in hearts treated with S1P vs. those treated with S1P+AG490. There was no change in the LV developed pressure. Combined GI and S1P in the recovery phase improved HR vs. controls (20.5±13.8 bpm, p=0.001 vs. controls, n=6).
- Conclusions: S1P activates the SAFE pathway by up-regulating STAT3 in the nucleus, whereas metabolic therapy by GI and S1P improved HR and contractility, thus suggesting principles of future therapy against AHF.

GROWTH FACTORS AND CARDIAC SIGNALING PATHWAYS

P2506 | BENCH
Metabolic and molecular approaches to treatment of de novo acute heart failure

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Purpose: Acute heart failure (AHF) is a clinical emergency, with high mortality and re-hospitalizations. Our model of de novo AHF examines the molecular survival activating factor enhancement (SAFE) pathway activated by sphingosine-1-phosphate (S1P), a component of HDL. S1P activates SAFE pathway by binding to its receptors which via the phosphorylation of signal transducer and activator of transcription 3 (STAT3) translocate to the nucleus and promote cell survival and improve recovery. We tested the involvement of the S1P-activated SAFE pathway in rat hearts subjected to de novo AHF. We also examined the combined effect of metabolic therapy by glucose-insulin (GI) and S1P.

Methods: AHF was induced by a reducing the perfusion pressure of the Langendorff perfused rat heart from 100cmmH2O to 23cmmH2O. Acute stress was imposed in the AHF phase by low glucose (2.5mmol/L) and elevating free fatty acids (FFA) (1.3mmol/L), thus creating combined hypotensive and metabolic stress. GI posed in the AHF phase by low glucose (2.5mmol/L) and elevating FFA (1.3mmol/L), thus creating combined hypotensive and metabolic stress. GI and S1P were added in the recovery phase following ischemia.

Results: S1P+GI improved the LV developed pressure (17.1 vs. 148.8 ± 26.4 BPM; p < 0.05 vs. GI; p < 0.001 vs. S1P+AG490; n=6) and improved LV ejection fraction (0.264 ± 0.01 vs. GI; p < 0.001 vs. S1P+AG490; n=6). STAT3 was increased (p<0.05) in the nuclear fraction in hearts treated with S1P vs. those treated with S1P+AG490. There was no change in the LV developed pressure. Combined GI and S1P in the recovery phase improved HR vs. controls (20.5±13.8 bpm, p=0.001 vs. controls, n=6).

Conclusions: S1P activates the SAFE pathway by up-regulating STAT3 in the nucleus, whereas metabolic therapy by GI and S1P improved HR and contractility, thus suggesting principles of future therapy against AHF.

P2509 | BEDSIDE
Myocardial redox state as a regulator of PPAR-gamma signalling in epicardial adipose tissue of patients with ischemic heart disease: insights from the Oxford CABG Bioresource

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Background: Epicardial adipose tissue (EAT) may have a role in heart disease. In additional 55 patients, EAT was incubated a) +/− H9c2 cardiomyocytes +/− NADPH-stimulated H9c2 cells. 4-HNE increased PPAR-γ activity in EAT in RAA (F) in an AMPK dependent manner (reversed by CC).

Methods: In 250 patients from the Oxford CABG Bioresource (OCB) undergoing elective CABG, we collected EAT and right atrial appendage (RAA) samples. In additional 55 patients, EAT was incubated a) +/− H9c2 cardiomyocytes +/− NADPH-stimulated H9c2 cells. 4-HNE increased PPAR-γ activity in EAT in RAA (F) in an AMPK dependent manner (reversed by CC)

Results: In OCB, higher levels of myocardial NADPH oxidase activity are associated with higher AdN gene expression in EAT. As shown in Figure, PPAR-γ (A) and AdN (B) gene expression were increased in EAT that was co-incubated with NADPH-stimulated H9c2 cells. 4-HNE increased PPAR-γ (C) and AdN (D) gene expression.

Conclusions: We propose for the first time a novel “inside to outside” signal from the myocardium to EAT: under conditions of increased myocardial oxidative stress 4-HNE induces a PPAR-γ mediated upregulation of AdN gene in EAT, which then exerts a paracrine inhibition of myocardial NADPH oxidase.
**P2511 | BENCH**

**Effects of adipokines in cardiac structure**


Heart failure (HF) represents a major and growing problem in the developed countries and several risk factors, such as obesity, are associated with its development. Obesity is defined as a pro-inflammatory state associated with an increased secretion of adipokines, which modulate the function of several organs and tissues. Cardiac adipose tissue segregates adipokines that can act in a paracrine and vasoactive manner on the myocardium, exerting direct effects in fibroblasts and cardiomyocytes. This project aimed at investigating the potential role of adipokines in cell proliferation and collagen production by cardiac fibroblasts and evaluating the crossstalk between collagen and the myocardium.

Experimentally, atria tissue from 25th week old ZSF1 lean (ZSF1 L, n=11) and ZSF1 obese (ZSF1 Ob, n=11) rats was used for the isolation of cardiac fibroblasts, as well as for obtaining conditioned medium from pericardial adipose tissue. Fibroblasts were cultured separately with adiponectin (100 nM) and adiponectin (10μg/ml). After 48h, BrdU assays and Sirius Red staining were performed in order to evaluate the effect of these adipokines in cell proliferation and collagen production, respectively. Moreover, adipokines in cardiac explants from 7-day-old Wistar rats and incubated with conditioned adipose tissue from obese and lean groups. After 24h of incubation, fibrosis and cross-section area of hematoxylin-eosin stained cardiomyocytes were assessed.

Incubation with adiponectin and adiponectin led to a significant increase in fibroblasts' proliferation in both groups (p=0.0496). In ZSF1 Ln, adiponectin led to a significant decrease in collagen secretion, while in ZSF1 Ob it increased collagen secretion (p=0.0054). Adiponectin significantly reduced collagen synthesis in both groups and decreased collagen secretion in ZSF1 Ln (p<0.001). Regarding the organotypic cultures, pericardial adipose tissue secreted from obese rats triggered a significant increase in fibrosis deposition (3.48±1.51% vs. 4.79±1.53%, p<0.05) and in the cross-section area of cardiomyocytes(100.7±18.98 μm² ± 111.25±4.02 μm², p<0.05), compared with the secretome from lean animals.

Adipokines produced by adipose tissue depots from obese animals seem to modulate the cardiac structure, through changes in extracellular matrix components and cardiomyocytes, features typically related to the appearance of diastolic dysfunction.

**P2511 | BENCH**

**Modulation of the transforming growth factor-beta effects in mitral valve prolapse**

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**Purpose:** The impact of angiotensin II receptor blockers (ARB) on extracellular matrix production by inhibition of the transforming growth factor-β (TGF-β) has been shown recently in vitro in cultured valvular interstitial cells obtained from patients with mitral valve prolapse (MVP) undergoing mitral valve repair. Our aim is to investigate the effect of ARB therapy on TGF-β serum level and volume (69.5 ± 15.1 mm Hg; p=0.009).

**Methods:** A total of 233 asymptomatic patients (mean age: 53.8±12.9) with severe mitral regurgitation (MR) due to mitral valve prolapse were enrolled in this retrospective, non-randomized, single-center study between 2009 and 2011. Concentrations of TGF-β1 and b2 in serum were determined by enzyme-linked immunosorbent assay. Standard echocardiography extended with assessment of MR volume and length and thickness of the mitral valve leaflets was performed in all patients (EchoP AC'08, GE).

**Results:** According to the case reports only 43 patients (18.5%) received losartan or telmisartan (study group). Most of the patients (190; 81.5%) did not receive any ARBs (control group). There were no significant differences between groups in age (54.8±11.3 vs. 52.6±12.9; p=0.26), other medical treatment (β-blockers: 39% vs. 36%, p=0.15; β-blockers: 0±1.6 vs. 0±1.4 mm, p=0.04; heart rate (82.6±14.4 vs. 74.2±15.7 b.p.m., p=0.0007) and blood pressure (135.5±15.1 vs. 142.2±15.1 mm Hg, p=0.009).

**TGF-β1 levels** despite large dispersion were significantly higher in subjects with MVP and significant MR (11.3±7.0 ng/ml) than in ARB group (16.1±15.1 μg/mL, p=0.0001), as well as TGF-β2 (7.6±7.0 ng/ml vs. 2.2±2.0 ng/mL, p=0.0005) and after recovery (0.9±0.45 mg/mL vs. 1.8±0.44 mg/mL, p=0.05). The molecular analysis showed that chronic stress significantly decreased the expression of PPAR-gamma in the WAT both after stress (fold-change to controls of 0.47±0.10, p=0.05) and after recovery (fold-change to controls of 0.68±0.04, p=0.05). Chronic stress significantly increased the levels of Lipocalin-2 (Lcn2; a recently described adipokine implied in inflammatory response) in WAT after stress (fold-change to controls of 5.45±2.32, p<0.01). The multiple sources of Lcn2 in WAT after stress and its immunohistochimistry was performed to ascertain the origin of this inflammatory molecule; Its analysis revealed Lcn2-positive infiltrating cells in the WAT after stress.

**Conclusion:** These data suggest that the deregulation of PPAR-gamma expres-
sion and the generation of a pro-inflammatory environment driven by Lon2 in the WAT might underlie stress-related insulin resistance.

P2514 | BENCH Investigation of action potential properties of native atrial and ventricular cardiomyocytes from the early embryonic to the adult stage allows the determination of the developmental stage of iPSCM

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Purpose: Cardiomyocytes (CM) derived from induced pluripotent stem cells (iPSCM) are promising candidates for cell therapy, drug screening and developmental studies. They possess immature electrophysiological properties, but an exact characterization of their developmental stage and subtype differentiation is hampered by a lack of knowledge of action potential (AP) properties of native CM from different developmental stages. Thus, we have investigated AP properties of murine CM and established a database that allows classification of iPSCM.

Methods: Hearts from 12.0-3.5 post coitum as well as 1 day, 3-4 days, 1-2 weeks, 3-4 weeks and 6 weeks post partum. Until day 12 p.c. AP recordings in left and right atria and at apical, medial and basal left and right ventricles were performed with glass microelectrodes in preparations of the whole chambers. Older ventricles were not sufficiently supplied if perfused into 150 μm thick viable tissue slices; recordings were performed in apical, medial and basal slices. AP recordings of iPSCM were performed in early- (day 11-16 of differentiation, EDS) and late (day 21-26, LDS) stage embryoid bodies.

Results: Atrial and postnatal development, APs of atria and ventricles under went significant changes. In both, atria and ventricles, the maximal diastolic potential (MDP) became more negative from days 9-10 p.c. to 1-2 weeks p.p. AP duration at 50% of repolarization (APD50) decreased considerably in atria and ventricles from days 9-10 p.c. to 3-4 weeks p.p. and increased slightly until 6 weeks. APD90 in atria and even more in ventricles decreased from 9-10 p.c. to 1-2 weeks p.p. and then increased until 6 weeks, resulting in a consistent decrease of APD50/90 ratio in atria and ventricles from days 9-10 p.c. to 6 weeks p.p. No significant differences were found between left and right atria and left and right ventricles. AP measurements in EDS and LDS iPSCM showed an increase of MDP and a decrease of APD50, APD90 and APD50/90 with time. The developmental stage and subtype of differentiation could be classified according to the data gathered from native CM. EDS iPSCM matched ventricular CM at days 9-10 p.c., LDS iPSCM matched ventricular CM at days 3-4 p.p.

Conclusions: Significant changes in AP morphology occur during pre- and postnatal murine heart development. This systematic analysis enables a classification of developmental stages and subtypes of adult and of stem cell-derived cardiomyocytes and supports that iPSCM undergo a physiological developmental process.

P2515 | BENCH TEMEM16A mediated calcium-activated chloride current synchronizes repolarization within mammalian ventricular myocardium

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Background: Recently identified TMEM16A is responsible for calcium-activated chloride current (ICl(Ca)) in the heart. Opening of this channel contributes to transient outward current; however, it can potentiate formation of delayed afterdepolarizations, especially in calcium-overloaded cells. The aim of this work was to study the role of ICl(Ca) in various regions of ventricular myocardium.

Methods: Electrophysiological studies were performed using conventional sharp microelectrode, whole-cell patch-clamp and action potential (AP)-clamp techniques in enzymbatically dissociated canine cardiomyocytes. ICl(Ca) was dis tended by perfusion of anthracene-9-carboxylic acid (9-AC, 0.5 mM). Western blot analysis and immunofluorescence of TMEM16A were carried out to visualize TMEM16A mediated calcium-activated chloride current synchronizes (patho)-physiological functions of afamin, we decided to identify phenotypes as-sociated with afamin by investigating transgenic mice overexpressing the human afamin. In this study, we tested whether the human afamin gene (patho)physiological functions of afamin, we decided to identify phenotypes as-sociated with afamin by investigating transgenic mice overexpressing the human afamin. In this study, we tested whether the human afamin gene

Conclusions: Our results show that selective inhibition of late INa is effective in suppressing arrhythmogenic markers (afterpotentials and TDR) associated with ventricular tachyarrhythmias.

P2517 | BENCH Plasma concentrations of afamin are associated with the prevalence and development of metabolic syndrome

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Aims: Afamin is a human plasma vitamin E-binding glycoprotein primarily expressed in the liver and secreted into the bloodstream. Since little is known about (patho)physiological functions of afamin, we decided to identify phenotypes associated with afamin by investigating transgenic mice overexpressing the human afamin and performing large-scale human epidemiological studies.

Methods and results: Transgenic mice overexpressing afamin revealed increased body weight and serum concentrations of lipids and glucose. We applied a fixed-effects meta-analysis using age- and sex-adjusted baseline and follow-
up investigations in the population-based Bruneck (n=826), SAPHIR (n=1499), and KORA F4 Studies (n=2060). Mean afamin concentrations were 62.5±15.3, 66.2±14.3, and 70.6±17.2 mg in Bruneck, SAPHIR and KORA F4, respectively. Per 10 mg/L increment in afamin measured at baseline, the number of metabolic syndrome components increased by 19% (incidence rate ratio (IRR)=1.19 (95%CI 1.16-1.21), p<0.0001). With the same afamin increment as used at baseline we observed an 8% gain in components between baseline and follow-up (IRR=1.08 (95%CI 1.06-1.10), p<0.0001). Afamin concentrations at baseline were highly significantly related to all individual metabolic syndrome components at baseline and follow-up. The observation was most pronounced for elevated waist circumference (OR=1.79 (95%CI 1.54-2.09), p<0.0001) at baseline and OR=1.46 (95%CI 1.31-1.63), p<0.0001 for change during follow-up and for elevated fasting glucose concentrations (OR=1.46 (95%CI 1.40-1.52), p<0.0001).

Conclusion: This study in transgenic mice and more than 5,000 participants in epidemiological studies in humans shows afamin being strongly associated with the prevalence and development of metabolic syndrome and all its components.

INTEGRATIVE PHYSIOLOGY

P2519 | BEDSIDE
Evaluation of cardiac axis changes related to obesity and aging by surface electrocardiogram and cardiac computed tomography
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Background: Changes in the cardiac electrical axis measured with surface electrocardiogram (EKG) are postulated to be related to changes in cardiac orientation. Obese individuals have a more leftward rotation of the electrical cardiac axis on surface EKG. Using cardiac computed tomography (CT) and the electrical cardiac axis in the frontal plane determined by surface EKG in young to middle aged individuals without structural heart disease. We then compared this with age matched obese individuals and older individuals without structural heart disease.

Methods: 124 patients who underwent CT coronary angiography were studied retrospectively. Group 1 included those between 30 and 60 years old with a normal body mass index (BMI). Group 2 included those between 30 and 60 years old who were obese. Group 3 included those greater than 60 years old with a normal BMI. Those with structural heart disease or thoracic deformities were excluded. In vivo cardiac orientation was determined along the long axis on CT and correlated with the electrical cardiac axis on surface EKG.

Results: In Group 1 (n=58), the mean CT axis was 23.9° (15.4° –56.2°) whilst the mean EKG axis was 51.8° (-11.6° - 125.8°), Pearson r value 0.12 (p<0.365). In Group 2 (n=36), the mean CT axis was 25.1° (-6.2° – 38.2°) whilst the mean EKG axis was 20.1° (1.3° -38.9°), Pearson r value 0.05 (p<0.806). In Group 3 (n=28), the mean CT axis was 34.4° (-9.1° – 51.8°) whilst the mean EKG axis was 34.4° (30.3°-30.8°), Pearson r value 0.26 (p<0.209). The CT and EKG axis had a more leftward rotation in Group 2 compared with Group 1 (p<0.0001). The CT axis however did not appear to be markedly different in Group 3 compared with Group 1 (p>0.05), whilst there was a significant difference in CT axis (p<0.031).

Conclusion: There is no simple relationship between an individual’s anatomical and electrical cardiac axis. Obese individuals have a more leftward rotation of both their axes when compared with age-matched normals, which may be secondary to elevation of the diaphragm. Older individuals had a more leftward rotation of both their axes when compared with age-matched normals, which may be secondary to elevation of the diaphragm.

P2520 | BENCH
Calcification of the coronary arteries identifies the least vulnerable vessel or lesion: a pathology study
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Aim: The aim of the current study is to assess if calcification of the coronary artery is able to predict the disease burden and vulnerability of a lesion.

Methods: Sudden coronary deaths were selected from the institute’s coronary artery pathology database based on the availability of a post-mortem X-ray per-formation. All of the specimens were evaluated and the correlation of the calcification area of the left main and three coronary arteries were measured. All coronary arteries were serially sectioned at 3-4 mm intervals, embedded in paraffin, and stained with H&E and Movat pentachrome. All histologic sections were evaluated for the type of lesion according to modified AHA criteria, quadrants of calcification, type of calcification (micro, focal, sheet, or nodular), and percentage stenosis.

Results: A total of 54 sudden cardiac deaths (207 vessels, 319 lesions) were diagnosed. Seventy lesions correlated with total and coronary CT calcium scores of type 4a (7 low Ca –5%, 19 medium Ca –5% - <20%, 18 high Ca –20%). Percentage calcification increased with age (low 45, medium 56,high 61 years; p=0.001) and was higher in diabetics (diabetes 42% vs. non-diabetes 14%; p<0.001). Fibrocalcific plaque was more frequently observed in the high-Ca compared to the low-Ca (low 7%, medium 24%, high 50%; p<0.001) and calcified sheets often involved 3 to 4 quadrants of the plaque. In contrast, prevalence of pathologic intimal thickening (PIT) and fibroatheroma was less in high-Ca compared with medium-Ca and low-Ca (low-Ca 65%, medium-Ca 39%,high-Ca 21%; p<0.001). Increasing calcification was associated with greater percent area stenosis, higher calcification burden and more severe types of calcification. The amount of calcification was a determinant of plaque vulnerability with 50% of plaque ruptures seen in low-Ca of the vessel, as compared to only 13% of cases with high-Ca of the vessel.

Conclusion: In a cohort of sudden coronary death cases, progression of coronary plaque is associated with higher percentage stenosis and coronary calcification. Moreover, calcification burden of the coronary artery is associated with increased risk of acute coronary events.

P2521 | BENCH
Prevalence and clinical features of microfistulas between coronary artery and left ventricle: Single center experience
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Objectives: Coronary artery fistulae are an infrequent malformation and the prevalence was reported approximately 0.1-0.4% according to previous studies. However, there is not enough study about microfistulas from coronary arteries to the left ventricle especially Turkish People. The purpose of this study was to evaluate the prevalence of microfistulas in our centre and to compare the staging of plaque calcification with presence of microfistulas, and increase in fibrocalcic plaques. Plaque rupture occurs most frequently in those with less calcification. In conclusion, coronary calcification burden of the coronary system is not associated with an increased risk of acute coronary events.

P2522 | BENCH
Human heart failure is associated with vascular channel mRNA degradation mediated by reduced HuR proteins
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Human heart failure has been associated with reduced cardiac sodium channel mRNA expression. Reduced SCN5A is thought to contribute to the arrhythmic risk in heart failure. The reduction in cardiac SCN5A mRNA abundance is reflected in circulating white cells that also express SCN5A. We hypothesized that reduced mRNA stability would contribute to reduced SCN5A mRNA abundance in heart failure. The SCN5A mRNA 3′-untranslated region (UTR) contains two sets of AU-rich elements (ARE), which mediate ARE-mediated mRNA decay. Hu proteins, members of the ARE-binding family of proteins, regulate human cardiac channel mRNAs. We hypothesized that this mRNA may have a more leftward rotation of their electrical cardiac axis only, which may reflect underlying conduction disturbances in this age group.

Conclusion: Our study found an overall 0.11% percent incidence of microfistulas. Furthermore, microfistulae are rare cardiac anomaly which sometimes cause cardiac symptoms and otherwise is detected during routine coronary angiography.

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References
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that circulating HU protein assessment may be useful in arrhythmic risk stratification, and HU protein elevation may help reduce arrhythmic risk in heart failure.

P2523 | BENCH
Metformin protects against cardiac mitochondrial dysfunction and improves insulin response in rats fed high fat diet
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A diet rich in fatty acids is known to induce insulin resistance and the metabolic syndrome. Furthermore, such diet may impair mitochondrial function and cardiac dysfunction may develop. Metformin (MET) is an antidiabetic drug and the first-line drug of choice for the treatment of type 2 diabetes. MET decreases hyperglycemia primarily by suppressing glucose production by the liver. The molecular mechanism of MET is incompletely understood; one suggested mode is activation of AMPK. However, another mechanism is inhibition of complex I and therefore increasing the ATP/ADP ratio. This mechanism contrasts with the positive effects of MET in type II diabetes. Therefore, we assessed the influence of MET treatment on cardiac and mitochondrial function during chronic high fat feeding.

Male Sprague-Dawley rats received either standard diet (SD - 9% cal. from fat) or high fat diet (HFD - 60% cal. from fat). Additionally, animals received an oral dose of MET (300mg/kg/d) or placebo. At the age of 23 weeks, cardiac function (echo-cardiography), glucose tolerance (i.e. GTT 2g/kg), cardiac mitochondrial function (respiratory capacity) and cardiac insulin response (Weston blot analysis) were assessed.

HFD induced body weight gain was significantly attenuated compared to MET (566±17 vs. HFD 629±8 vs. NC-MET 545±16 vs. HFD-MET 561±18g). This reduction in weight gain through MET was also confirmed by a decrease in epididymal fat. Echocardiography revealed no long term influence of either HFD or MET on cardiac morphology, systolic and diastolic function (E/E: 16.7±1.6 vs. 17.2±0.5 vs. 14.1±0.9 vs. 17.0±0.6).

Whole body glucose tolerance was attenuated with HFD and treatment with MET did not improve this loss in sensitivity (AUC: 775±41 vs. 1051±85 vs. 914±89 vs. 1184±56). Furthermore, cardiac insulin response was significantly reduced with HFD suggesting cardiac insulin resistance. This decrease in insulin sensitivity was abolished with MET (AUC 2.1±0.7 vs. 1.4±0.14 vs. 1.38±0.15 vs. 1.35±0.10).

Concomitantly, with cardiac insulin resistance, cardiac mitochondrial function was also deteriorated. Maximal respiratory capacity of isolated mitochondria was significantly reduced with HFD. Treatment with MET was able to compensate for this metabolic decrease (316±36 vs. 216±19 vs. 437±147 vs. 319±23; succinate: 550±5 vs. 440±38 vs. 661±163 vs. 635±47; NAD/mg). Coupling between ATP production and oxygen consumption was unaffected by HFD and MET.

Oral treatment with metformin improves cardiac insulin sensitivity and prevents mitochondrial dysfunction triggered by high fat diet.

P2524 | BENCH
Long-term serotonin reuptake inhibitor administration enhances diet-induced obesity and impairs leucocyte recruitment into adipose tissue in mice
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Purpose: Metabolic syndrome leads to aseptic inflammation of visceral adipose tissue and insulin resistance and strongly associates with atherosclerotic disease. Increased food intake promotes adipocyte growth and recruitment of pro-inflammatory immune cells to the adipose niche. We recently observed that platelet-derived serotonin promotes neutrophil recruitment to sites of acute inflammation and therefore hypothesized that serotonin affects traits of the metabolic syndrome.

Methods: Wild-type (WT) in the presence and absence of a selective serotonin reuptake inhibitor (SSRI, fluoxetine) or tryptophan hydroxylase (Tph-) 1−/− mice - only by 72.2±1% in Tph1−/− mice (p=0.01). Food intake assessed by metabolic caging did not differ between the groups. Tph1−/− mice showed improved insulin tolerance and glucose tolerance was significantly impaired. These data suggest an insulin secretion deficiency. While macrophage content in visceral adipose tissue was similar, that of CD8+ T-cells was reduced from 20.1±1.1% in WT to 7.6±1.9% (p=0.001) in Tph1−/− mice and 14.6±2.3% (p=0.01) in mice treated with SSRI.

Conclusion: Lack of platelet-derived serotonin in Tph1−/− mice protects from diet-induced obesity and pro-inflammatory leucocyte recruitment into adipose tissue. These results provide the basis for treated mice and points to a possible use for the treatment of metabolic syndrome.

P2525 | BENCH
Inducible, heterozygous Ryr2 knockout mice reveal a key role for SR Ca2+ release in cardiac metabolism
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Background: Heart failure is a multi-faceted condition characterized by numerous functional lesions including contractile dysfunction and metabolic inflexibility. The cardiac ryanodine receptor (RYR2) Ca2+ release channel plays an essential role in excitation contraction and is functionally reduced by up to 50% in multiple models of heart disease including both hypertensive and diabetic cardiomyopathies. Given that RYR2 dysfunction is known to decrease oxidative energy metabolism, RYR2 is poised to have an additional role in pacing cardiomyocyte metabolism. To test which aspects of heart failure may be downstream of RYR2 dysfunction, we have developed a model whereby RYR2 protein is reduced to a stable 50% level in cardiomyocytes. The overall objective of our research is to test whether a 50% reduction in RYR2 signalling can be an upstream driver of cardiac pathology and metabolic dysfunction.

Methods and results: We generated a conditional, haploinsufficiency model for RYR2 function by crossing mice with only one floxed Ryr2 allele with a cardiac specific, tamoxifen-inducible Cre deleter mouse line. This deletion led to a stable 50% decrease in Ryr2 mRNA and RYR2 protein levels a month after tamoxifen injection. Despite decreased RYR2 levels, no significant changes were observed in cardiac output measured by echocardiography or in the contraction of isolated cardiomyocytes. Only minor decreases in cardiac output were observed during ex vivo perfusion of isolated working hearts. However, we did observe a significant decrease in glucose oxidation during working heart perfusion despite no significant reductions in ATP levels or in the oxidation of other metabolic substrates. Unbiased proteomic and metabolomic analyses identified significant decreases in key TCA cycle intermediates and a compensatory up-regulation of Ca2+ sensitive metabolic proteins. Targeted biochemical analysis revealed further mechanistic details linking partial RYR2 ablation to metabolic changes. Collectively these results indicate that a chronic, stable 50% decrease in RYR2, even without alterations in heart function, is sufficient to alter cardiac cellular metabolism and impede the use of glucose as a substrate for oxidative ATP metabolism.

Conclusions: These results provide evidence that RYR2 is critically involved in several aspects of oxidative metabolism in cardiomyocytes. Furthermore, these findings show that RYR2 dysfunction is able to disrupt cardiac metabolism regardless of its affects on excitation-contraction, which suggests a role for RYR2 dysfunction in mediating cardiac dysfunction in heart disease.

P2526 | BENCH
Direct load- and heart rate-independent control of ventricular contractility by a distinct population of vagal preganglionic neurons
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Purpose: To identify vagal preganglionic neurons which directly control left ventricular contractility using an animal model to fix loading and heart rate conditions, applying this model to pharmacological activation of chemically identified inhibition of neurons from the dorsal motor nucleus of the vagus nerve (DMVN).

Methods: Male Sprague-Dawley rats (380-420g) were anaesthetised with pentobarbital sodium (induction 60 mg/kg i.p.; maintenance 15–20 mg/kg i.v.) and artificially ventilated. Femoral artery and vein were cannulated to monitor arterial pressure (ABP) and for the infusion of fluid and drugs. Following C1 spinal transection and atenolol (2mg/kg/h i.v.) treatment to remove sympathetic tone, vasopressin (30pg/kg/h i.v.) was infused to restore ABP. Transthoracic atrial pacing (confirmed with lead II ECG) and fixed loading conditions allow the maximum first differential of left ventricular pressure (LVdP/dt max) to be used as a load independent index of contractility. With the prone head down position, the diaphragm was exposed and isolated with a well-muscled but non-loaded left ventricle to be used as the load independent index of contractility. With the prone head stereotaxically fixed, the dorsal surface of the brainstem was exposed. Bilaterally, three discrete regions (0.5 mm apart) of vagal preganglionic neurones were transduced with a lentiviral vector (LV)
Results: Comparisons of allele frequencies for 2462 subjects with CHD and 2284 controls by the chi-square test revealed that the rs84977574 of the phosphatase and actin regulator 1 gene (PHACTR1) (P = 0.0001, FDR = 0.0002) and rs4977574 of the CDKN2B antisense RNA 1 (CDKN2BAS1) (P = 0.0042, FDR = 0.0031) were significantly associated with CHD. Multivariable logistic regression analysis with adjustment for age, sex, body mass index, smoking status, and the prevalence of hypertension, diabetes mellitus, and dyslipidemia revealed that the rs9369640 (P = 0.0006; odds ratio, 0.73; dominant model) and rs4977574 (P = 0.0043; odds ratio, 1.26; recessive model) were significantly associated with CHD. The minor G allele of rs9369640 was protective against CHD, whereas the minor G allele of rs4977574 was a risk factor for this condition. Next, a relation of 15 polymorphisms to MI was examined among 1822 subjects with MI and 2284 controls. Comparisons of allele frequencies by the chi-square test revealed that the rs9369640 (P = 0.0005, odds ratio, 0.70; dominant model) and rs4977574 (P = 0.0004; odds ratio, 1.37; recessive model) were significantly associated with MI.

Conclusions: The rs9369640 of PHACTR1 and rs4977574 of CDKN2BAS1 may be susceptibility loci for CHD and MI in Japanese individuals.

COMPUTED TOMOGRAPHY IN ASYMPTOMATIC HIGH RISK SUBJECTS

P2530 | BEDSIDE Is metabolic syndrome predictive of coronary artery disease burden, and prognosis beyond its individual components? Results from the CONFIRM Registry

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Background: Metabolic Syndrome (MeTS) is shown to increase the risk of cardiovascular disease and mortality. However, it is not yet known if MeTS has any additive prognostic value beyond its individual risk factors (RF). The purpose of this study is to compare the prevalence, severity of coronary artery disease (CAD) and prognosis of patients with and without MeTS.

Methods: The study cohort consisted of 27,125 consecutive individuals who underwent 64 detector row CTA at 12 centers from 2003 to 2009. Patient with known CAD, unknown statin use or unavailable lipid profile were excluded. MeTS was defined as per NCEP/ATP III criteria. We focused on 3900 patients who had measured RF for MeTS and were not on statin therapy. Of these, 690 patients met the criteria of MeTS. Propensity matching was performed for age, sex, smoking status and family history of premature CAD with patients without MeTS (no-MeTS) with 0, 1, 2 MeTS RF. CAD was defined as none, non-obstructive (1–49% stenosis), or obstructive (≥50% stenosis). Major adverse cardiac events (MACE) was defined as MI, acute coronary syndrome, all cause mortality and late revascularization. MACE was assessed by risk-adjusted Cox proportional hazards models.

Results: MeTS group had higher rates of obstructive 1, 2 and 3-vessel/left main disease compared to no-MeTS group with 0 or 1 RF (13.8 vs. 8.8%, 4.5% vs. 2.4% and 2.3% vs. 0.9%, respectively; p < 0.01). However, presence of obstructive 1, 2 and 3-vessel left main disease was not significantly different between MeTS and no-MeTS group with 2 RF (13.8 vs 10.5%, 4.5% vs 2.8% and 2.3% vs 1.3%, respectively; p = nonsignificant). At 2.2 year follow up. MeTS group had higher MACE compared to no-MeTS subgroups with 0 or 1 RF (4.4% vs 1.8%; P < 0.01). There was no statistically significant difference in MACE between MeTS group and no-MeTS subgroup with 2 RF (4.4% vs 3.2% P = NS).

Conclusion: The prevalence and severity of CAD as well as MACE rate are significantly higher in MeTS group compared to no-MeTS group. However, these differences are not significant when comparing MeTS group with no-MeTS subgroup with 2 RF. These findings challenge the prognostic value of MeTS as a syndrome beyond the sum of its components.
stable coronary artery disease (CAD) establish the assessment of pretest probability (PTP) as the first diagnostic step. However, the endorsed method for calculating PTP accounts only for age, sex and typicality of symptoms. Recently, a new score was proposed (CAD Consortium 2), which adds cardiovascular risk factors to the calculation of PTP. The aim of this study was to compare the accuracy of the two methods in patients undergoing coronary CT angiography (CCTA) for suspected CAD.

Methods: We evaluated 889 patients (370 men, age 58±12 years) without known CAD undergoing CCTA for stable chest pain. Data on diabetes, hypertension, smoking and dyslipidemia were collected prospectively. Chest pain was classified as typical, atypical or non-specific according to standard criteria. Each patient’s PTP was calculated as recommended by the ESC 2013 guidelines, and with the CAD consortium 2 score. Obstructive CAD was defined as coronary stenosis ≥50% on 64-slice dual-source CCTA.

Results: Obstructive CAD on CCTA was present in 144 patients (16.2%). The observed prevalence was significantly lower than the predicted by the ESC 2013 method, but very similar to the CAD consortium estimate (Figure). The C-statistic for CAD consortium 2 was significantly better than for the ESC 2013 method (0.760 vs. 0.725, p=0.006). Using the CAD consortium 2 score would result in a net reclassification improvement of 17.6% (p=0.005).

Conclusion: Our multiple randomized trial demonstrated CCS increased by more than 30% irrespective of a significant reduction of LDL-cholesterol by pitavastatin. There was no significant difference in the progression of CCS among intensive or standard statin therapy without/with EPA. But this increase in CCS was not associated with cardiovascular event during follow-up.

P2534 | BEDSIDE
Effects of intensive lipid lowering therapy on coronary plaques composition in patients with acute myocardial infarction. Assessment with serial coronary CT-angiography
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Background: Statins have been shown to possess beneficial pleiotropic effects with favorable effects on the cardiovascular system including modulation of the inflammatory response and stabilization of the vulnerable plaque. We sought to assess the effects of early aggressive statin treatment on plaque composition in patients with acute myocardial infarction (AMI), using serial assessment with coronary CT-angiography (CTA)

Methods: In a prospective randomized blinded endpoint trial patients with AMI were randomized to an intensive lipid lowering treatment receiving statin loading with 80 mg rosuvastatin followed by 40 mg daily or standard statin therapy according to current guidelines. Patients were assessed with a 64-slice CTA at baseline and after 12 months with evaluation of plaque burden and composition. Main outcome measure was changes in plaque composition from baseline to 12 months follow-up.

Results: In total, 140 patients with AMI were randomized and plaque composition was assessed in 96 patients. In the intensive care group LDL-level was median 1.3 [0.9-1.5] mmol/l at 12 months follow-up and 2.0 [1.7;2.4] mmol/l in the usual care group, p=0.001. Overall, plaque composition changed after 12 months with an increase in necrotic core volume of 26.8 (±122.1) in the intensive care group and 25.2 (±80.1) in the usual care group, p=0.94. Total dense calcium plaque volume increased 11.1 (±39.6), corresponding to 23%, in the intensive care group and decreased -0.4 (±26.6) in the usual care group, p=0.001.

Conclusion: Early aggressive lipid lowering therapy significantly increases dense calcium volume in patients with AMI. It might be possible that an increase in plaque density demonstrates a plaque stabilizing effect.
The sensitivity of CT A for stenosis in asymptomatic diabetic patients evaluated by coronary computed tomography angiography

M. Nishio, Y. Ueda. Osaka Police Hospital, Osaka, Japan

Background: In the asymptomatic but high-risk patients of coronary artery disease (CAD), the appropriate use of coronary CT angiography (CCT A) remains uncertain. We examined the characteristics of CAD by CCT A among the asymptomatic type 2 diabetic patients without known or suspected CAD and major cardiovascular events of those patients.

Methods: Consecutive patients (n=168) with asymptomatic type 2 diabetes without known or suspected CAD who underwent CCT A were enrolled. The CAD was classified by CCT A as normal-mild, moderate, or severe. The patients were followed-up for MACE for 1062.372 days. Medical treatment and other cardiovascular measurements such as carotid artery atherosclerosis, peripheral stiffness, and LV diastolic dysfunction, were also evaluated.

Results: Severe stenosis was detected in 90 (54%) patients. 16 (9.5%) patients underwent PCI or CABG following this CCT A result. Other patients underwent optimal medical therapy. Among all patients, 3 major cardiovascular events occurred. In patients with moderate stenosis, one patient developed sudden death due to unknown origin. In patients with severe stenosis, 1 patients with OMT alone developed brain infarction, and 1 patient with PCI underwent reintervention for stent restenosis. Other cardiovascular measurements appeared associated with moderate to severe coronary stenosis.

Conclusion: More than half of asymptomatic type 2 diabetic patients had moderate to severe coronary stenosis. Treatment with OMT with or without coronary intervention in those patients may lead to good outcome.

P2538 | BENCH

New algorithm for calculation of the continuum of coronary artery calcification progression

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Purpose: Coronary artery calcification (CAC), a marker of atherosclerosis, can be determined by computed tomography (CT) and demonstrates an exponential percentile increase depending on age and gender. We analyzed the changes in age and gender dependent percentile distribution of CAC during a five year follow-up period in a general population cohort based on repeated electron beam CT (EBCT).

Methods: In 1633 men and 1848 women (age 45–75 years), repetitive EBCT was performed 5.1±0.3 years apart. Our conjecture was that a subject’s CAC increases with age along the given percentile at 10. Therefore, we estimated log(CAC(t1) + 1) using only the baseline CAC quartile Q(10), sex, and adjusted for age by time between scans (time) from log(CAC(t1) + 1) = I(Q(t0)) + (t/10) (age + 15.6) (table 1). Results were for men, the estimated age at which a given percentile reaches a given value of CAC is plotted in Fig. 1A, corresponding prediction limits are given for CAC 400. For example, if the CAC value in a man corresponds to the 40th percentile, CAD risk factors for above outcome.

Results: For men, the estimated age at which a given percentile reaches a given value of CAC is plotted in Fig. 1A, corresponding prediction limits are given for CAC 400. For example, if the CAC value in a man corresponds to the 40th percentile, CAD risk factors for above outcome.

Conclusion: The new algorithm for calculating the continuum of coronary artery calcification progression allows the estimate of the age at which threshold of risk are reached and enables a distinct discussion of the physician with the patient concerning his life expectancy of CAC progression.

Figure 1. Percentile distribution of CAC.

Table 1

<table>
<thead>
<tr>
<th>CAC</th>
<th>Q(10)</th>
<th>Sex</th>
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<td>40</td>
<td>10</td>
<td>5</td>
<td>65</td>
</tr>
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<td>400</td>
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Figure 1: Male Cohort

Conclusion: The new algorithm for calculating the continuum of coronary artery calcification progression allows the estimate of the age at which threshold of risk are reached and enables a distinct discussion of the physician with the patient concerning his life expectancy of CAC progression.

P2537 | BENDSIDE

Prevalence and severity of coronary artery disease among asymptomatic diabetic patients evaluated by coronary computed tomography angiography

M. Nishio, Y. Ueda. Osaka Police Hospital, Osaka, Japan

Background: In the asymptomatic but high-risk patients of coronary artery disease (CAD), the appropriate use of coronary CT angiography (CCT A) remains uncertain. We examined the characteristics of CAD by CCT A among the asymptomatic type 2 diabetic patients without known or suspected CAD and major cardiovascular events of those patients.

Methods: Consecutive patients (n=168) with asymptomatic type 2 diabetes without known or suspected CAD who underwent CCT A were enrolled. The CAD was classified by CCT A as normal-mild, moderate, or severe. The patients were followed-up for MACE for 1062.372 days. Medical treatment and other cardiovascular measurements such as carotid artery atherosclerosis, peripheral stiffness, and LV diastolic dysfunction, were also evaluated.

Results: Severe stenosis was detected in 90 (54%) patients. 16 (9.5%) patients underwent PCI or CABG following this CCT A result. Other patients underwent optimal medical therapy. Among all patients, 3 major cardiovascular events occurred. In patients with moderate stenosis, one patient developed sudden death due to unknown origin. In patients with severe stenosis, 1 patients with OMT alone developed brain infarction, and 1 patient with PCI underwent reintervention for stent restenosis. Other cardiovascular measurements appeared associated with moderate to severe coronary stenosis.

Conclusion: More than half of asymptomatic type 2 diabetic patients had moderate to severe coronary stenosis. Treatment with OMT with or without coronary intervention in those patients may lead to good outcome.

P2535 | BEDSIDE

Diagnostic accuracy of coronary computed tomography angiography and single-photon emission computed tomography in renal transplantation candidates

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Purpose: Before patients with end stage renal disease are listed for renal transplantation, screening for coronary artery stenosis is frequently needed. Despite low sensitivity and specificity non-invasive modalities are preferred. The aim of this study was to compare the diagnostic accuracy of coronary artery stenosis with single-photon emission computed tomography (SPECT), coronary computed tomography angiography (CCT A), and their combination (hybrid scan) using invasive coronary angiography as reference.

Methods: We prospectively evaluated patients with chronic kidney disease stage 5 referred for renal transplantation by CCT A, SPECT and invasive coronary angiography. According to our pre-defined protocol, interpretation of CCT A and SPECT were merged into an integrated hybrid imaging result. Significant stenosis was defined as more than 50% diameter stenosis by invasive coronary angiography. Data were analyzed by two experienced cardiologists and nuclear medicine experts blinded to patient data and results.

Results: We enrolled 138 patients with mean age 54 (SD: ± 11) years, 68% males and 32% on dialysis. Median time from study inclusion to invasive coronary angiography was 34 days (10th and 90th percentiles: 24 and 48 days). The overall prevalence of significant CAD by invasive angiography was 21.7%. Sensitivity, specificity and area under the receiver-operating curves (ROC) are listed in table 1. Method comparison revealed significant higher for the hybrid scan than for SPECT (p < 0.05) whereas the accuracy by hybrid scan and CCT A was similar.

Conclusions: With coronary angiography as gold standard, a hybrid scan of CCT A and SPECT had higher diagnostic accuracy than CCT A. Combination of CCT A and SPECT may be recommended as preferred diagnostic standard for preoperative evaluation before renal transplantation.

P2536 | BEDSIDE

Coronary computed tomography angiography in asymptomatic high-risk patients: non-calculating and total coronary plaque burden predict outcome

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Purpose: To prospectively assess the value of coronary computed tomography angiography (CTA) in asymptomatic patients with high-risk of coronary artery disease estimated by risk factors for adverse outcome. The aim of this study was to compare the diagnostic accuracy of coronary artery stenosis with single-photon emission computed tomography (SPECT), coronary computed tomography angiography (CCT A), and their combination (hybrid scan) using invasive coronary angiography as reference.

Methods: 711 consecutive asymptomatic patients (61.8y, 40.1% females) with chronic kidney disease stage 5 had a hazard ratio (HR) of 6.49 (95%CI: 1.63-25.76, p < 0.013) for CAC progression. The mean follow-up period was 2.65 years (up to 8 years). MACE rate was 0% in asymptomatic type 2 diabetic patients without known or suspected CAD and major cardiovascular events of those patients.

Results: More than half of asymptomatic type 2 diabetic patients had moderate to severe coronary stenosis. Treatment with OMT with or without coronary intervention in those patients may lead to good outcome.

Conclusion: The new algorithm for calculating the continuum of coronary artery calcification progression allows the estimate of the age at which threshold of risk are reached and enables a distinct discussion of the physician with the patient concerning his life expectancy of CAC progression.

Figure 1: Percentile distribution of CAC.
P2539 | BEDSIDE
Epicardial fat volume. A novel risk biomarker for the subclinical coronary artery
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Background: Epicardial fat volume (EFV) measurement, using cardiac computed tomography (CT) has been shown to be a reliable marker of coronary atherosclerosis, and greater EFV is associated with coronary artery disease (CAD). However, little is known on the relation between the amount of EFV and the severity of coronary atherosclerosis in identifying high risk patients with subclinical CAD. The aim of this study was to investigate the relationship between EFV and severity of coronary artery disease measured by CT.

Methods: We retrospectively analyzed data of 600 individuals with suspected coronary artery disease who were referred for evaluation with cardiac CT from 2007 to 2012. Subjects who had history of primary coronary intervention or coronary artery by-pass graft were excluded. Thickness of epicardial adipose tissue (EAT cm3), was measured on noncontrast multiplanar reformat images with parasternal short axis view at basal, mid-ventricular and apical levels and horizontal long axis view as the sum of the EAT areas with 2mm thick from the whole heart. CAD severity was determined by the presence of significant coronary stenosis (>50% luminal narrowing of at least one major coronary artery), high coronary artery calcium score (CACS >100) and plaque characteristics (any plaque causing significant stenosis and/or vulnerable plaques), in the subsequent CT angiography.

Results: In the finally studied population of 434 consecutive individuals, 155 (35, 7%) had atherosclerotic coronary artery disease and 279 (64, 3%) of them were normal. Overall, 75.2% were male; mean age was 58±18 years with a mean EAT 155, 54 cm3. Patients with coronary atherosclerosis had significantly greater mean EAT compared to normals (p<0.01). Linear regression analysis revealed that the incidence of significant stenosis, atherosclerotic plaque and high calcium score increased with EFV (p<0.01).

Conclusion: EFV measured by 64-slice CT scanning, was closely associated with significant CAD and its measurement might be used in addition to CACS CT angiography as an early indicator of increased risk of coronary atherosclerosis.

P2540 | BENCH
Glycemic status and coronary atherosclerosis in asymptomatics: evaluation by coronary CT angiography

Objectives: We investigated the prevalence, extent, and severity of coronary artery disease (CAD) in normal glucose regulation (NGR), prediabetes and diabetics of varying duration using dual-source coronary computed tomography angiography (CCTA) in individuals without chest pain.

Methods: We consecutively enrolled 2758 patients without CAD undergoing CCTA, and divided into NGR, prediabetes, and diabetes groups based on their diabetes history, fasting plasma glucose and glycosylated hemoglobin levels. 1446 diabetic patients were reclassified into three groups according to the duration of diabetes: <5 years, 5–10 years, and ≥10 years. We compared the various results of CCTA among groups.

Results: Diabetic patients showed significantly greater degrees of coronary artery calcium score (CACS), athromer burden obstructive score (ABOS), segment involvement score (SIS), and segment stenosity score (SSS), compared with NGR or prediabetes individuals (p<0.001 for all). Longer duration of diabetes was associated with higher rate of CAD (p<0.001), and proportionately greater degree of CACS, ABOS, SIS, and SSS on CT scans (p<0.001 for all). Diabetes, even newly diagnosed or with the duration of less than 5 years was associated with an increased risk of CAD as compared with NGR individuals [diabetes duration <5 years (odds ratio (OR) 2.15, 95% confidence interval (CI) 1.29-3.57, p<0.001); 5–10 years (OR 3.481, 95% CI 1.850-6.472, p<0.001); >10 years (OR 9.152, 95% CI 5.557-15.072, p<0.001); although no differences were found between NGR and prediabetes individuals.

Conclusions: In asymptomatic individuals, the prevalence, extent and severity of CAD are significantly higher in patients with long-standing diabetes. However, prediabetes was not associated with an increased risk of CAD.

PET AND SPECT FOR VISUALISATION OF INFLAMMATION

P2542 | BENCH
18F-anti-VCAM-1 nanobody for PET/CT imaging of inflamed atherosclerotic plaque
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Purpose: Vascular cell adhesion molecule-1 (VCAM-1) is expressed in inflamed atherothrombotic atherosclerotic lesions and is a potential target for the molecular imaging of vulnerable plaques. A mouse/human cross-reactive anti-VCAM-1 nanobody (Nb) has previously described with 99mTc-coupled 99mTc-hexamethylene diacetate (HMDA) for its ability to image VCAM-1 expression by PET/CT in a mouse model of atherosclerosis.

Methods: The anti-VCAM-1 Nb (cAbVCAM1-5) was labeled using the prosthetic group N-succinimidyl-4-18F-fluorobenzoate (18F-SFB) and purified by size exclusion chromatography. In vitro cell binding studies using TNF-α stimulated bEND3 cells were carried out to assess the functionality of the tracer. In vivo µPET/CT imaging was performed at 2h30 post-injection using 20-30-week-old ApoE−/− mice on a Western diet (Group 1) and normally fed C57BL6 control mice (n=3 per group), which were injected with 18F-anti-VCAM-1 Nb. To demonstrate the specificity, additional ApoE−/− mice were injected with 18F-labeled non-targeting control Nb or with 70-fold excess of unlabeled anti-VCAM-1 Nb. Ex vivo evaluation (n=6 per group) of plaque uptake in different aorta segments based on lesion-extension index (score 0: 0.68±0.10, score 1: 1.18±0.36, score 2: 1.49±0.37, score 3: 1.84±0.38%ID/g). In the Group 1, lesion-to-heart ratio and lesion-to-blood ratios were high (11.2 and 3.13, respectively). Conclusion: Mouse/human 18F-anti-VCAM-1 Nb allows non-invasive PET/CT imaging of VCAM-1 expression in atherosclerotic plaques in a mouse model and may represent an attractive tool for imaging vulnerable atherosclerotic plaques in patients.

P2543 | BEDSIDE
Quantitative 18F-Fluorodeoxyglucose positron emission Tomography/Computed Tomography for the discrimination of infective from non-infective implantable cardiac electronic device pocket complications
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Purpose: Confirmation of implantable cardiac electronic device (ICED) pocket infection can be difficult when patients present with mild or non-specific symptoms that may or may not be due to infection. The aim of this study was to investigate the utility of 18F-Fluorodeoxyglucose positron emission tomography with combined computed tomography (18F-FDG PET/CT) in the early diagnosis of ICED pocket infection.
Methods: Eighteen patients with possible ICED pocket infection were evaluated using 18F-FDG PET/CT and blood markers of infection prior to deciding on the clinical need for ICED extraction. These patients included those with mild symptoms (localized pain in the region of the ICED generator pocket, with or without mild erythema) in the absence of definite features of infection (significant erythema, abscess formation, purulent discharge or erosion). 18F-FDG PET/CT values from these patients were correlated to the persistence or progression of clinical signs (the current clinical gold standard for diagnosing ICED infection), and to separate cohorts of patients: patients with definite infection (n=20), and control subjects (n=35) undergoing 18F-FDG PET/CT scanning for other indications. An SUV(max) of >2 on 18F-FDG PET was considered abnormal.

Results: Nine (50%) patients with possible infection had increased 18F-FDG uptake in the region of the ICED generator pocket. Infection was confirmed on clinical grounds in 8 out of these 9 patients; these patients subsequently underwent ICED extraction. A pathogen was recovered from extracted samples in 7 out of 8 patients (88%). Patients with confirmed infection (n=28) had significantly higher 18F-FDG uptake around the ICED pocket compared to non-infected cases and controls (SUVMax 4.75 [2.85-5.55] vs 1.35 [1.30-1.85] vs 1.0 [1.25-1.70] respectively, p<0.001). The sensitivity and specificity of the 18F-FDG scan to detect infection using SUV max was 93% [CI 76%-99%] and 87% [CI 73%-95%] respectively.

Conclusions: ICED infection may first manifest as mild symptoms in the region of the generator pocket. 18F-FDG PET/CT is sensitive and specific for the discriminating of infective from non-infective ICED pocket complications.

P2544 | BEDSIDE
Differential aortic inflammation and calcification in abdominal aortic aneurysm and atherosclerosis
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Purpose: The vascular biology of both abdominal aortic aneurysm (AAA) and atherosclerosis remain incompletely understood. We hypothesized that inflammation and calcification may have a differential contribution to the pathogenesis of both diseases.

Methods: In 63 patients with asymptomatic AAA and 19 age- and sex-matched patients with atherosclerosis, we measured inflammation and calcification using 18F-fluorodeoxyglucose (18F-FDG) positron and computed tomography (PET-CT). Inflammation and calcification were quantified using 18F-FDG target-to-background ratios (TBR) and Agatston scores.

Results: Thrombus within AAA had low 18F-FDG uptake compared to the wall of the aneurysm (p<0.0001). 18F-FDG uptake was higher in the aneurysmal aorta than in non-aneurysmal aorta (mean TBR 2.23±0.45 vs. 2.12±0.45, p<0.02). Compared to patients with atherosclerosis only, both aneurysmal and non-aneurysmal aortic uptake was higher in AAA patients (n=18; mean TBR 2.23±0.45 vs. 1.68±0.21, p<0.001; abdominal aortic mean TBR 2.23±0.45 vs. 1.68±0.21, p>0.001) in patients with AAA. Calcification in aneurysmal aorta was greater than in non-aneurysmal segments (Agatston 4918 [2901-8008] vs. 1017 [139-2226], p<0.0001). There was no significant difference between total aortic calcification between patients with AAA and atherosclerosis (Agatston total aorta 5136 [3297-9360] vs. 3735 [1425-8261], p=0.180).

Conclusion: Aortic inflammation is more pronounced in AAA than in atherosclerosis. Moreover, even with adjacent atheroma, aortic inflammation is more marked suggesting an exaggerated systemic vasculopathy in patients with AAA. This is further supported by the findings of increased aortic calcification in aneurysmal disease: a marker of end-stage necrotic inflammation.

P2545 | BEDSIDE
Impact of liver transplantation on the progression of myocardial sympathetic denervation assessed by 123I MIBG imaging in familial amyloid polyneuropathy

Patients with familial amyloid polyneuropathy (FAP) V30M-TTR have documented myocardial sympathetic denervation assessed by 123I-metabolodobenzylguanidine (MIBG) imaging which correlates closely with the severity of neurological involvement. Liver transplantation is widely used to attenuate the progression of the disease, but it is still contradictory its impact on the evolution of cardiac involvement. We aimed to evaluate the impact of liver transplantation on the progression of myocardial denervation in V30M-TTR FAP patients. To assess the impact of liver transplantation on the progression of cardiac denervation, the late H/M uptake ratios of the images performed prior to liver transplantation (n=100) were compared with the H/M uptake ratios of the images acquired subsequently (n=87). It was found that the progression of disease, evaluated by the decrease in late H/M as a function of time, was significantly attenuated from the time of liver transplantation. In fact, until the time of liver transplantation the late H/M ratio declined 0.47/year (Pearson R=0.469, p<0.001, Spearman’s Rho=0.379, p<0.001). After transplantation no statistically significant correlation was observed between the elapsed time and the decrease in the late H/M ratio.

Conclusion: Liver transplantation permits stabilization of cardiac denervation in V30M-TTR FAP. After transplantation, the values of the late H/M uptake ratios remain stable over time, without recovery or further deterioration. Thus, it is crucial that the treatment is carried out at an early stage of the natural history of the disease.

P2547 | BEDSIDE
Perspective and prognostic value of myocardial sympathetic denervation assessed by 123I MIBG scintigraphy in familial amyloid polyneuropathy

Introduction: Familial amyloid polyneuropathy (FAP) V30M TTR is an autosomal dominant disease characterized by progressive impairment of sensory-motor and autonomic nerve fibers. Myocardial scintigraphy with 123I-metabolodobenzylguanidine (MIBG) is a noninvasive method for quantification of cardiac sympathetic denervation. We sought to evaluate the progression of cardiac sympathetic denervation in serial 123I MIBG imaging and to examine its impact on the prognosis.

Methods: Observational study of V30M TTR mutation carriers subject to an-
PET and SPECT for visualisation of inflammation

P2548 | BEDSIDE Useful parameter of myocardial fatty acid metabolism and blood flow mismatch for the diagnosis and the detection of myocardial injury in active cardiac sarcoidosis

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Purpose: F18-FDG-PET is recently reported to be useful for the diagnosis and its detection of active myocardial inflammation in patients with cardiac sarcoidosis (CS). In contrast, the assessment of myocardial injury and left ventricular function are clinically important for the future risk management. The aim is to clarify whether FDG uptake as a parameter of active inflammation/metabolism is associated with myocardial injury detected by I-123 BMIPP (BMIPP) and Tl-201 (TL) which reflect fatty acid metabolism and myocardial blood flow, respectively.

Methods: Thirty patients with suspected CS who underwent FDG-PET/CT and BMIPP-TL exams per patient, showed that the only independent predictors of death were age (HR=1.05, p=0.01), and heparin infusion 15 min before FDG administration. PET and SPECT images were acquired at 60 min post injections and analyzed with Scape software for visualisation. Metabolites were mapped to metabolic pathways. Significant differences were calculated after normal distribution test.

Conclusions: We studied 34 patients with coronary artery calcification (CAC), 17 with severe CAC (score >250) and 17 with moderate CAC (score >250) and compared them with 26 controls with no calcification. The metabolic profiling analysis revealed that severe CAC was significantly associated to the presence of low density plaque (31% vs. 18%, p=0.02), spotty calcification (24% vs. 11%, p=0.01) and HSR (22% vs. 10%, p=0.01). The thickness of CAC was also correlated with the number of low-density plaque and HRP, and coronary artery calcium score as well as age, body mass index, visceral adipose tissue (VAT) area. Multiple logistic analysis revealed that severe CAC was an independent predictor of death (HR 2.3, 95% CI: 1.2-4.5, p<0.01). With increasing duration of symptoms there was a progressive decrease in the early H/M (ratio <1.74; HR=13.72, 95% CI 4.89-38.49, p<0.001). Regarding the late H/M ratio, patients belonging to the 2nd or 3rd tertile had a risk of death 6 times higher than those belonging to the 1st tertile (late H/M ratio <1.00). The ROC curve analysis showed the AUC was 0.66 (0.59 to 0.73, p<0.01) and sensitivity and specificity to detect HRP were 65% and 61% with cut off value of 5.6mm.

P2550 | BENCH Apoptosis is a potential mechanism for severe calcific coronary artery disease

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Background and aim: Severe coronary calcification, irrespective of luminal stenosis, may cause limiting symptoms, but does not respond to conventional management policies. Little is known about its exact pathophysiology. The aim of this study is to identify metabolic disturbances that distinguish calcific coronary artery disease.

Methods: We studied 34 patients with coronary artery calcification (CAC), 17 with severe CAC (score >250) and 17 with moderate CAC (score >250) and compared them with 26 controls with no calcification. The metabolic profiling analysis of patients serum was conducted using untargeted ultra-performance liquid chromatography-tandem mass spectrometry coupled to magnetic separation. Metabolic separation was achieved using an Acquity UPLC system and detection using a Xevo G2 Q-TOF MS. Features were then extracted using MarkerLynx package. Metabolic structural assignment was accomplished based on tandem MS spectra. Pathway analysis included, calculating correlation coefficients, and using CytoScape software for visualisation. Metabolites were mapped to metabolic pathways using the KEGG database. Multivariate Statistical Analyses were performed using the SIMCA-P+ 12 software.

Results: A total of seven different dysregulated sphingomyelins were detected, all consistently lower in severe CAC compared with controls (p=0.000001 – 0.01). Sphingomyelins were not different between moderate CAC and controls, but significantly lower in severe CAC compared with moderate CAC (p=0.000006 – 0.01). We found the same lipid composition in patients with non valvular atrial fibrillation (AF). Of the four metabolomes of LAA described (Chicken-wing (CW), Cauliflower, Cactus and Windsock), CW metabolome is associated with lowest stroke incidence as compared to other three (non-

P2549 | BEDSIDE Utility of epicardial adipose thickness by echocardiography as a predictor for coronary plaque vulnerability determined by coronary CT angiography

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Objective: The aim of this study is to investigate the relationship of EPA (Epicardial adipose tissue) by echocardiography and high risk plaque evaluated with coronary CT angiography.

Methods: We enrolled 406 patients (mean age 64 years, 231 men). Echocardiography was simultaneously measured on the free wall of the right ventricle from a parasternal long-axis view at end-systole. High risk coronary plaque (HRP) components were defined as the presence of non-calcified plaque (NCP) including low-density plaque (<50 HU), spotty calcium and positive remodeling (remodeling index <0.5). In accordance with a ROC curve analysis, patients were assigned into two groups: thin (<5.6 mm) or thick (≥5.6mm) EAP group.

Results: Compared to the thin EAP group, the thick EAP group had a higher prevalence of low density plaque (31% vs. 18%, p<0.01), positive remodeling (33% vs. 42%, p=0.02), spotty calcification (24% vs. 11%, p<0.01) and HSR (22% vs. 10%, p=0.01). The thickness of CAC was also correlated with the number of low-density plaque and HRP, and coronary artery calcium score as well as age, body mass index, visceral adipose tissue (VAT) area. Multiple logistic analysis revealed that severe CAC was an independent predictor of death (HR 2.3, 95% CI: 1.2-4.5, p<0.01). With increasing duration of symptoms there was a progressive decrease in the early H/M (ratio <1.74; HR=13.72, 95% CI 4.89-38.49, p<0.001). Regarding the late H/M ratio, patients belonging to the 2nd or 3rd tertile had a risk of death 6 times higher than those belonging to the 1st tertile (late H/M ratio <1.00). The ROC curve analysis showed the AUC was 0.66 (0.59 to 0.73, p<0.01) and sensitivity and specificity to detect HRP were 65% and 61% with cut off value of 5.6mm.

P2551 | BEDSIDE A study of LAA morphology in rheumatic heart disease

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Introduction: Assessment of Left atrium appendage (LAA) morphology by computerized tomography (CT) has mass spectrometry to be important in prediction of stroke in patients with non valvular atrial fibrillation (AF). Of the four morphologies of LAA described (Chicken-wing (CW), Cauliflower, Cactus and Windssock), CW morphology is associated with lowest stroke incidence as compared to other three (non-

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PET and SPECT for visualisation of inflammation / Perfusion imaging for prognosis

Chicken wing (non CW). Non-CW morphologies have been shown to confer additional risk of stroke in non valvular AF. No study has compared LAA morphology and stroke prevalence in Rheumatic valvular AF and compared with non valvular AF.

**Methodology:** We studied 106 consecutive patients with AF who attended the outpatient clinic. All patients underwent CT for evaluation of LAA morphology. Observations - Mean age of patients was 56.5 years and 50.9% were males. 15 (14.15%) had history of previous stroke. Out of 106 patients, 49 (46.22%) had rheumatic valvular affection, 6 (12.24%) of them had history of stroke. 57 patients had non-valvular AF. 9 (15.76%) had history of stroke. Clot in LAA was noted in the 28 of 106 (26.4%) patients.

Amongst rheumatic valvular AF patients, 32 (65.3%) had CW morphology and 4 (12.5%) patients had history of stroke. 17 patients (34.7%) had non-CW morphology of LAA and had history of stroke. Amongst the 57 non valvular AF patients, 28 (49.1%) had CW morphology; 1 (3.57%) had history of stroke. 29 patients had non-CW morphology (50.9%) and 8 (27.5%) had h/o stroke.

**Conclusions:** Findings of our observational study indicate low prevalence of stroke in non valvular AF patients with CW morphology (3.57%) as compared to non CW morphologies (27.5%). In rheumatic valvular AF group, prevalence of stroke in CW morphology was 12.5%, which is 3.5 fold higher as compared to non valvular AF group. In non CW morphology the prevalence of stroke was comparable, in both the groups. CHADS score is not applicable to rheumatic valvular AF and LAA morphology also does not help significantly based on our study. Assessment of stroke risk in rheumatic valvular heart disease remains a challenge.

**PERFUSION IMAGING FOR PROGNOSIS**

**P2553 | BEDSIDE**

*Non-stenotic coronary lesions: how to manage these patients*

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Coronary angiography has diagnostic limitation in identifying non-stenotic coronary lesion (NSCL) responsible for ischemia. Myocardial perfusion defects in patients (pts) with NSCL have often been unreliably considered by invasive cardiologists as being “false positive”. We evaluated a prognostic value of gated SPECT MPI in unselected group of the pts with NSCL over a 24 month period of follow-up.

170 pts (115 males, 67.6%; age 42-68 years; mean age 56.4±9.2 years) with NSCL (stenosis of 50% or less of LAD and 70% or less of any other coronary artery or its major branches, FFR>0.80) were enrolled into the study. Retrospective analysis of 86 pts with NSCL and subsequent positive MPS performed within 6 months from the time of coronary angiography (study group) and 84 pts with normal scan results (control group) was performed. Follow-up period was for 24 months from the time of MPI or up to the time of major coronary event (MCE) - fatal or non-fatal myocardial infarction or cardiac death.

Over a two-year follow-up, approximately 11% of the pts in study group had MCE as compared to 3.2% in the control group (P<0.01). Abnormal MPI, EF <35% and high levels of hs-CRP were independent predictors for MCE in the study group.

In multivariable analysis only an abnormal MPI remained to be an independent predictor regardless of size or severity of perfusion abnormalities (P<0.005).

Pts with NSCL on coronary angiography and myocardial perfusion defects have relatively high event rate (11%) of MCE over a period of 24 months from the time of MPI. So, we highly recommend gated SPECT MPI to be obligatory performed in all cases of NSCL to avoid life-threatening coronary complications in forthcoming future.

**P2555 | BEDSIDE**

*Frequency and long-term prognostic importance of myocardial perfusion deficits in patients with non-specific chest pain admitted to a coronary care unit with a suspected acute coronary syndrome*


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**Purpose:** To assess the frequency and long-term prognostic importance of stress-induced myocardial perfusion deficits in pts with non-specific chest pain (NSCP) admitted to the coronary care unit (CCU) with a suspected acute coronary syndrome (ACS).

**Methods:** During a 21-month period all pts discharged from the CCU without evidence of present or prior coronary artery disease and without other medical conditions that could cause the chest pain were prospectively screened to indentify potential pts with NSCP. Eligible pts underwent careful history taking and a clinical evaluation to rule out conditions that could cause the chest pain were prospectively screened to indentify potential pts with NSCP. Eligible pts underwent careful history taking and a stress myocardial perfusion scintigraphy (MPS) within four weeks. MPS studies were interpreted without knowledge of clinical findings. MPS was defined as positive when a horizontal or down-sloped ST depression of ≥1 mm. Follow-up was 5.1±3.4 years. We recorded cardiac complications (CC, non fatal myocardial infarction or cardiac mortality) and coronary revascularization (R) in women and men.

**Results:** Stress test was positive in 407 (16.9%) patients, in 15.9% of women and 17.5% of men. CC (6.5% vs 2.3%; p=0.005) and CC + R (11.8% vs 4.8%; p=0.001) were more frequent in men with positive stress test than men with a negative stress test. These differences were not observed in women. In the multivariate analysis we observed that CC and CC + R were more frequent in men with positive stress test (shh: 2.8 [CI 95%: 1.3 to 6.3]; shr: 2.5 [CI 95%: 1.4 to 4.4], respectively) than in women with negative stress test.

**Conclusions:** Men with normal gated-SPECT of myocardial perfusion but with positive stress test have a worse prognosis than women with the same results. Sex and abnormal stress tests are variables that may modify the good prognosis of a normal myocardial perfusion scan.
Chronic kidney disease and stress left ventricular systolic function in adenosine stress myocardial perfusion imaging predict future cardiovascular events.

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Background: Adenosine stress myocardial perfusion imaging (MPI) is widely applied for detection of coronary ischemia as well as exercise MPI. Chronic kidney disease (CKD) has been considered to be a strong predictor for cardiovascular events. However, the precise predictors of future events evaluated by using combination of indices from adenosine stress testing and clinical characteristics remain to be uncertain. The objective of this study is to determine the predictors from adenosine stress MPI that will affect the future cardiac events in patients suspected of coronary artery disease.

Methods: A total of 1,256 consecutive patients (male/female 801/455, age 71±11 years) suspected of coronary artery disease underwent adenosine MPI. The outcomes of interest were the hard events (cardiovascular death and sudden death) and the non-fatal events (heart failure worsening, acute coronary syndrome, aortic dissection and aneurysm). Stress left ventricular ejection fraction (LVEF), summed stress score (SSS), summed rest score (SRS), age and presence of clinical risk factors (diabetes mellitus, dyslipidemia, hypertension and CKD) were evaluated.

Results: A total of 25 cardiovascular deaths and 70 cardiovascular non-fatal events occurred over 778±354 days of follow-up. Univariate Cox analysis showed that predictors for total cardiac deaths were age (hazard ratio 1.03; P<0.05), stress LVEF (hazard ratio 0.96 P<0.001), SSS (hazard ratio 1.06; P<0.001), SRS (hazard ratio 1.05, P<0.001), presence of DM (hazard ratio 1.53; P<0.05), and presence of CKD (hazard ratio 2.86; P<0.001). Multivariate Cox analysis showed that presence of CKD (hazard ratio 2.32; P<0.001), stress LVEF (hazard ratio 0.96 P<0.001), and SSS (hazard ratio 1.03; P<0.05) were the independent predictors of total cardiovascular events.

Conclusions: Adenosine stress MPI and SSS and stress LVEF in adenosine stress ECG-gated myocardial perfusion SPECT imaging were the independent and strong predictors for the future cardiovascular events especially in the presence of CKD.

P2559 | BEDSIDE

Simultaneous PET/MR imaging for predicting left ventricular function after myocardial infarction.

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Objectives: Myocardial PET imaging using the radiolabeled glucose analog 18F-FDG delineates regional glucose utilization as a marker of viable cardiomyocytes. Early revascularization including late gadolinium enhancement (LGE) technique identifies increased extravascular space in areas of infarction and scar. In this study we measured simultaneously regional myocardial 18F-FDG uptake and LGE in patients early after acute myocardial infarction (AMI). Both parameters were compared with changes of left ventricular function after revascularization.

Methods: 28 patients with primary AMI underwent initial simultaneous PET/MRI 5 to 7 days after PCI. Follow-up imaging by MRI only was performed in 20 patients about 6 months after PCI. In a first step, myocardium was defined as “PET normal” based on the established threshold of more than 50% 18F-FDG uptake compared to remote myocardium or as “MR non-transmural” when LGE transmurality was less than 50%. In a second step, variable thresholds for regional 18F-FDG uptake or LGE transmurality were evaluated.

Results: In the “PET normal” group the EF was higher compared to the “PET abnormal” group both early after acute MI as well as at follow-up (EF initial: 48±10% vs. 39±8%; p<0.05; EF follow-up: 49±11% vs. 63±2%; p<0.03), while no differences for the EF were found between “MR non-transmural” and “MR transmural” patients (EF initial: 48±19% vs. 52±11%; p=NS; EF follow-up: 48±12% vs. 55±10%; p=NS). The improvement of the regional wall motion was significantly better in the “PET normal” vs. the “PET abnormal” group (-0.1±0.7 vs. -1.0±0.8, p<0.05), while no significant difference was found when patients were analyzed based on MRI transmural criteria (-0.1±0.8 vs. 0.5±0.8, p=NS). 7 patients (35%) showed discrepant findings, i.e. myocardium was “abnormal” based on PET and “non-transmural” based on MR. At follow-up, the regional myocardial function of these patients was inferior compared to the PET normal/MR non-transmural group (0.3±0.5 vs. 1.6±0.5, p<0.003) and showed no difference compared to the PET abnormal/MR transmural group (1.9±0.8, p=NS). Based on our results, thresholds which are associated with LV function recovery are a regional 18F-FDG uptake of more than 50% and a LGE transmurality of less than 25%.

Conclusions: The simultaneous assessment of LGE transmurality and 18F-FDG uptake in patients after AMI using a hybrid PET/MR system is feasible. The established PET “viability” parameter predicts accurately the regional LV function outcome after AMI, however, the established MRI parameter of LGE transmurality might not apply for these patients.

P2560 | BEDSIDE

Quantitative assessment of myocardial perfusion in the detection of significant coronary artery disease

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Purpose: Recent studies have demonstrated the improved diagnostic accuracy for detection of coronary artery disease (CAD) when myocardial blood flow (MBF) is quantified in absolute terms. One of the challenges, however, is the lack of uniformly accepted cut-off value for detecting hemodynamically significant coronary

objective...
Aortic valve stenosis (AVS) is characterized by pressure overload and myocardial hypertrophy by aortic valve replacement (AVR) is able to reverse changes in contractile efficiency. The present study was conducted to investigate myocardial energetics and diastolic function. 

**Methods:** A total of 330 patients (mean age 61.9 ± 7.1 years, 192 men) with a pre dominantly intermediate pre-test likelihood of CAD underwent both quantitative [15O]H2O PET and invasive coronary angiography in conjunction with fractional flow reserve (FFR) measurements. A stenosis > 90% and/or an FFR < 0.80 was considered obstructive, while a stenosis ≤ 30% and/or an FFR > 0.80 was considered non-obstructive.

**Results:** Hemodynamic significant CAD was diagnosed in 116 (41%) out of 281 patients that fulfilled the study criteria for definition of CAD. Resting perfusion was 1.00 ± 0.26 and 0.92 ± 0.23 mL/min-1-g-1 in regions supplied by non-stenotic and significantly stenosed vessels, respectively (p < 0.001). During physiological stress, perfusion increased to 3.26 ± 1.05 and 1.78 ± 0.74 mL/min-1-g-1, respectively (p < 0.001). The optimal stress perfusion cut-off value was 2.3 mL/min-1-g-1. The corresponding value for myocardial flow reserve (MFR) was 2.50. With these cut-off values, sensitivity, specificity and accuracy of hyperemic MFR for the detection of functionally relevant CAD were 87, 84, and 85%, respectively, at a per patient basis and 85, 83 and 84% at a per vessel based analysis. The corresponding values for the MFR were 84, 73 and 77% at a per patient level and 79, 80 and 80% at a per vessel level. In addition, there was a significant impact of gender and age on the MFR (p < 0.001). 

**Conclusion:** The optimal cut-off values for detecting flow limiting stenoses were 2.3 mL/min-1-g-1 and 2.5 for hyperemic MBF and MFR, respectively. For diagnosing hemodynamically significant CAD, absolute hyperemic MBF was superior to MFR. Quantitative MBF measurements using [15O]H2O PET provide high diagnostic performance, but both gender and age should be taken into account.

**Purpose:** Aortic valve stenosis (AVS) is characterized by pressure overload induced left ventricular hypertrophy (LVH). It is unclear whether hypertrophied hearts of AVS patients are energetically compromised and reversal of cardiac hypertrophy by aortic valve replacement (AVR) is able to reverse changes in contractile efficiency. The present study was conducted to investigate myocardial energetics and diastolic function.

**Methods:** Ten AVS patients were included (normal coronary arteries, mean age 62.1 ± 10.7 years, 7 male). Echocardiography and cardiopulmonary exercise test were performed prior to AVR and repeated after 4 months to assess peak aortic valve gradients and exercise parameters, respectively. Changes in left ventricular mass (LVM) and volumes were assessed by cardiovascular magnetic resonance (CMR) imaging and simultaneously low-dose adenosine-[15O]H2O positron emission tomography (PET) was performed to obtain MVO2. Next, MEE was calculated and compared with 14 healthy controls (mean age 48 ± 11 years, 9 male).

**Results:** Four months after AVR, peak aortic valve gradient decreased from 88 ± 20 to 24 ± 12 mmHg (p < 0.001), as well as LVM index from 104.4 ± 21 to 74 ± 15 g/m² (p < 0.001). MVO2 significantly decreased from 0.11 ± 0.03 to 0.09 ± 0.02 mL/min-1-g-1 (p = 0.02), which was comparable to the MVO2 observed in controls (0.10 ± 0.02 mL/min-1-g-1). In addition, cardiac work significantly decreased from 15439 ± 2631 to 10774 ± 2446 mmHg mL (p = 0.001). During physiological stress, hyperemic MFR was 84 ± 15%. Consequently, AVR resulted in a significant improvement in MEE from 32 ± 7 to 37 ± 5.5% (p = 0.02). A significant correlation was observed between absolute changes in MEE (ΔMEE) with absolute changes in cardiac work (ΔCardiac work) (r = 0.74, p = 0.02) and absolute changes in peak VO2 (r = 0.67, p = 0.03).

**Conclusions:** At 4 months follow-up, the detrimental effects of AVS are partially reversed by AVR in patients with normal coronary arteries and preserved ejection fraction, evident from regression of left ventricular hypertrophy and improvement of MEE.

**Purpose:** Several studies reported that preventive percutaneous coronary inter-
Conclusion: MC-G mapping is a promising tool to identify a subset of heart failure patients who have narrow QRS but would benefit from CRT with subsequently an excellent clinical outcome.

P2556 | BEDSIDE
Utility of the ST-segment deviation score in the risk prediction of patients with suspected acute myocardial infarction

Purpose: ST-segment deviation score (STDS), a summation of all ST-segment deviations from baseline in a standard 12-lead ECG, has shown to correlate with mortality in patients with acute coronary syndrome. However, it is unknown whether these findings can be generalized to the clinical important setting of unselected patients presenting with acute chest pain, in which the early and reliable detection of patients at higher risk still presents an unmet clinical need.

Methods: In this prospective diagnostic study STDS was determined in 1404 consecutive patients presenting to the emergency department (ED) with symptoms suggestive of acute myocardial infarction. Primary endpoint was the occurrence of all-cause mortality within 30 days and 730 days. Patients with left ventricular hypertrophy or bundle branch block were excluded. The STDS was defined as the sum in millimeters (1mm=1mV) of the absolute value of ST-segment deviations in all 12 leads of the first recorded ECG.

Results: Fourteen (1%) patients died within 30 days and 65 (5%) within 730 days. STDS at presentation in the highest tertile (>4.7mm) compared to the intermediate or lowest tertile (≤2.7mm) was associated with an increased risk for death in the ensuing 30 days (HR 4.5, p<0.007) and 360 days (HR 2.4, p<0.001). Multivariate analysis showed that initial STDS levels remained an independent predictor of death within 30 days after adjustment for high-sensitive cardiac troponin T levels at presentation (HR 5.0, p<0.008) or TIMI-risk score (HR 5.5, p<0.001).

Conclusions: STDS, a simple and easily feasible clinical tool, helps in the risk stratification of unselected patients presenting with acute chest pain to the ED, as it independently and reliably predicts the short and long term mortality in this clinically important setting.

ClinicalTrials.gov number, NCT00470587

P2557 | BEDSIDE
St-segment deviation score in the early diagnosis of acute myocardial infarction

Purpose: The ST-segment deviation score (STDS) has been invented for the early detection of ischemic signs in a standard 12-lead-electrocardiography (ECG) in patients with symptoms suggestive of acute myocardial infarction (AMI).

However, little is known about the optimal cutoff-values or the time of measurement in the repolarisation-phase.

Methods: We conducted a prospective study to examine the diagnostic accuracy of the STDS in 1404 consecutive patients who presented with symptoms suggestive of AMI to the emergency department. Patients with left ventricular hypertrophy or bundle branch block were excluded. The STDS was defined as the sum in millimeters (1mm = 1 mV) of the absolute value of ST-segment deviations in all 12 leads of the initially recorded ECG. The STDS was determined at several timepoints during the electrocardiographic phase of repolarisation. The final diagnosis was centrally adjudicated by two independent cardiologists.

Results: AMI was the adjudicated final diagnosis in 248 (18%) patients (206 NSTEMI, 42 STEMI). The diagnostic accuracy of the STDS-measurements obtained at presentation, as quantified by the area under the receiver operating characteristic curve (AUC) was best at J-point (0.67; 95% confidence interval 0.64-0.69) with decreasing accuracies during later phases of significantly (AUCs ranging between 0.55-0.65, p = 0.05 for comparisons). E.g. a cutoff value of 8.4 mm in the STDS resulted in a positive likelihood ratio of 3.5 for the diagnosis of AMI. In the setting of a non-diagnostic ECG at presentation (n=1130, 80%), the AUC of STDS-measurements at J-point tended to be superior to later sites with an AUC of 0.54 (95%CI 0.51-0.57; p = 0.05 for all comparisons). The optimal cutoff value for the STDS in this clinically important subgroup was 2.7 mm with a sensitivity of 70% and a specificity of 41%.

Conclusions: The STDS in acute chest pain patients for the early diagnosis of AMI is determined best at J-point and, in conjunction with clinical examination and biomarker findings, might be of particular help to select patients without a diagnostic ECG but at higher risk of having an AMI.

ClinicalTrials.gov number, NCT00470587

P2558 | BEDSIDE
Clinical usefulness of a QRS scoring system for estimating rapid progression of myocardial infarction in patients with ST-segment elevation myocardial infarction
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Purpose: Several studies have found increased mortality in patients with complete right bundle-branch block (CRBBB) and concomitant cardiovascular disease, and this conduction disturbance has been shown to be a strong predictor of prognosis in the CA patients.

Methods: In this prospective diagnostic study STDS was determined in 1404 consecutive patients presenting to the emergency department (ED) with symptoms suggestive of acute myocardial infarction. Primary endpoint was the occurrence of all-cause mortality within 30 days and 730 days. Patients with left ventricular hypertrophy or bundle branch block were excluded. The STDS was defined as the sum in millimeters (1mm = 1mV) of the absolute value of ST-segment deviations in all 12 leads of the first recorded ECG.

Results: Fourteen (1%) patients died within 30 days and 65 (5%) within 730 days. STDS at presentation in the highest tertile (>4.7mm) compared to the intermediate or lowest tertile (≤2.7mm) was associated with an increased risk for death in the ensuing 30 days (HR 4.5, p<0.007) and 360 days (HR 2.4, p<0.001). Multivariate analysis showed that initial STDS levels remained an independent predictor of death within 30 days after adjustment for high-sensitive cardiac troponin T levels at presentation (HR 5.0, p<0.008) or TIMI-risk score (HR 5.5, p<0.001).

Conclusions: STDS, a simple and easily feasible clinical tool, helps in the risk stratification of unselected patients presenting with acute chest pain to the ED, as it independently and reliably predicts the short and long term mortality in this clinically important setting.

ClinicalTrials.gov number, NCT00470587

P2559 | BEDSIDE
Complete right bundle-branch block is a marker of worse outcome in survivors after out of hospital cardiac arrest
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Purpose: Several studies have found increased mortality in patients with complete right bundle-branch block (CRBBB) and concomitant cardiovascular disease, and this conduction disturbance has been shown to be a strong predictor of prognosis in the CA patients.

Methods: Of 395 consecutive patients with out-of-hospital CA for the last 18 months, 46 patients (31 male, 67.12 years old) without evidence of terminal non-cardiac disease, trauma,airway obstruction,drowning, or intoxication were re-admitted to hospital. They were divided into following two groups: 1) with CRBBB; 2) without CRBBB. Baseline demographic, clinical and electrocardiographic characteristics were analyzed and the survival was evaluated. CRBBB on electrocardiography was defined as QRS prolongation ≥120ms, rSR, complex in lead V1 or V2, and a slurred S waves in lead I, aVL, and V5 or V6.

Results: CRBBB was identified in 15 patients. There was mostly no significant difference in baseline characteristics including the presence of ischemic heart disease between two groups, but QRS and QTc duration were longer in patients with CRBBB than those without CRBBB (164±29 vs 120±32 [ms]; P = 0.01, 474±45 vs 441±43 [ms]; P = 0.03, respectively). The time until return of spontaneous circulation was not different (31.5±16.5 vs 24.3±15.2 [min]; P = 0.15), but patients with CRBBB had marked lower in >30 days survival than those without CRBBB (6.7 vs 45.2%, log-rank test; P = 0.01).

Conclusions: Presence of CRBBB after resuscitation might suggest the poor prognosis in the CA patients.

Kaplan-Meyer curve for CA.

Conclusion: We can estimate the extent of RP in patients with STEMI using QRSscore/Time.
P2569 | BEDSIDE
Prediction of atrial fibrillation recurrence in patients with pulmonary vein isolation by P-wave signal-averaged electrocardiogram
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Background: The noninvasive methods for predicting atrial fibrillation (AF) recurrence after the first pulmonary vein isolation (PVI) has not been well described. The aim of this study was to assess the usefulness of the P-wave signal-averaged electrocardiogram (P-SAECG) in predicting the recurrence of AF after the first PVI.

Methods: P-SAECG was recorded within 1 week, before (pre) and after (post) the first PVI session in consecutive 87 idiopathic AF patients (EF > 50%, BNP < 200pg/ml). Filtered P-waves (Pd20) and root mean square voltages in last 20 msec of the filtered P-wave (LP20) were measured.

Results: After the PVI session, the mean follow-up periods was 12±7 months. During the follow-up period, 22 of 87 patients experienced recurrence of AF (n=11, Paroxysmal-AF, n=11, Persistent-AF). Pre-PFD or Pre-LP20 was not significantly different between non-recurrence group and recurrence group. However, Post-PFD of paroxysmal-AF recurrence group was significantly shorter than non-recurrence group and Post-LP20 of paroxysmal-AF recurrence group was significantly larger than non-recurrence group. And then, Post-PFD was significantly longer in the case of LPV re-conduction. As a result, the Post-LP20/LP20 ratio was significantly higher than non-recurrence group (0.024±0.009 vs. 0.015±0.007, p<0.05).

Conclusion: The post-LP20/LP20 ratio may be useful for predicting a paroxysmal-AF recurrence in idiopathic AF patients with PVI.

P2570 | BEDSIDE
Hypertension and the electrocardiogram: a study in a large primary care telematics database in Brazil
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Purpose: The 12-lead electrocardiogram (ECG) is the most readily available non-invasive test for the detection of cardiac disease in primary care. The detection of preclinical cardiac abnormalities is a key clinical step in hypertension management, and several guidelines for hypertension treatment [1-3] recommend an ECG in hypertensive patients to improve risk prediction. The objective of this study is to assess the prevalence of ECG abnormalities in patients with hypertension who were attended at primary care centers in Brazil.

Methods: In this observational and retrospective study, all 12-lead standard digital ECGs analyzed by cardiologists of a public telemedicine service in Brazil, from January to December 2011, were assessed. This service attends primary care of 660 cities in our state. ECGs were sent by remote healthcare professionals through the internet analyzed by cardiologists who are trained and experienced in the analysis and interpretation of ECG. The prevalence of ECG abnormalities in patients with hypertension was assessed.

Results: During the study period, 82,125 primary care patients with hypertension underwent ECG (mean age 60.8±13.5 years, 63.7% females). The most common comorbidities besides hypertension were diabetes (14.2%), smoking (11.4%), obesity (23.5%), hyperlipidemia (7.0%) and Chagas disease (5.6%). Regarding the ECG analysis, 48.3% of them had no abnormalities, and the mean number of abnormalities per patient was 0.91±1.1 (range 0-9). Regarding the rhythm, 2.9% had atrial fibrillation or flutter, 3.2% ventricular premature beats, 2.4% supraventricular premature beats and 0.6% were pacemaker users. Left bundle branch block (LBBB) was observed in 2.4% of the ECGs, incomplete LBBB in 1.8%, right bundle branch block (RBBB) in 4.6% and left anterior hemiblock in 8.7%. First degree atrioventricular block was found in 2.5%, second and third degree in less than 0.1% each. There was electrocardiographic evidence of left ventricular and atrial hypertrophy in 5.2% and 3.2% of patients, respectively, and pathologic Q waves in 1.5%. Non-specific repolarization abnormalities were observed in 29.4% of the patients.

Conclusion: The most common abnormalities were non-specific repolarization abnormalities, RBBB, LBBB, left ventricular hypertrophy, premature beats and atrial fibrillation.

P2571 | BEDSIDE
Selective beat averaging to evaluate ventricular repolarization adaptation: in this large sample of primary care patients with hypertension, ECG abnormalities were observed in more than 50% of patients. The most common abnormalities were non-specific repolarization abnormalities, RBBB, LBBB, left ventricular hypertrophy, premature beats and atrial fibrillation.

P2572 | BENCH
Assessment of the ST dynamics by telemetry ECG method to determine the indications for emergency angioplasty after thrombolysis
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Purpose: To investigate the value of ST-segment dynamics in telemetry ECG monitoring in patients with acute coronary syndrome with ST segment elevation (ACS STE) to determine the indications for emergency coronary angioplasty.

Methods: The study included 25 patients with ACS STE, 17 men and 8 women with signs of effective thrombolysis, performed within the first 3 hours of the disease onset. All patients in the Cardiac Intensive Care Unit conducted under telemetric ECG using complex “Astrokard® - Telemetry” with an analysis of the ST segment dynamics on the 12-lead automatically with subsequent medical verification.

Results: Mean age 56.5±1.8 years. The average time from the start of angina attack to TLT was 2:56±0.33 h. The patients were divided into 2 groups. Group 1 included 14 patients (56%) who did not register the new ST-segment deviation from the contour in the process of monitoring. Patients in this group have not been patients with emergency coronary angioplasty. The delayed coronary artery occlusion led to the coronary artery stenosis without signs of thrombosis. Hospital mortality was absent. Group 2 included 11 patients (44%), in which after 98±12 minutes of the effective TLT the re-elevation of ST segment by 1 mm or more in 2 contiguous leads, lasting more than 1 minute, were fixed. Re-elevation of ST segment was preceded the angina attack recurrence by 15±7.5 minutes. The emergency coronary angiography was performed in patients of group 2. In 8 patients (72.7%) the signs of thrombosis of the infarct-related coronary artery (TIMI 0-1) were revealed and emergency angioplasty with restoration of blood flow in the TIMI 2 in 25% of patients and TIMI 3 in 75% of patients were performed. Re-thrombosis of infarct-related coronary artery in group 2 was significantly more frequent than in patients of group 1 (p<0.0001). In 4 of these patients with three-vessel disease angioplasty of the infarct-related artery was not performed due to technical reasons. Mortality in the group 2 was 9% (1 patient), and significantly higher than mortality in the group 1 (p<0.01).

Conclusions: Re-elevation of ST segment by 1 mm or more is a reliable diagnostic criterion of infarct-related coronary artery re-thrombosis. Telemetric ECG allows to identify the patients for whom an emergency percutaneous coronary intervention after the effective systemic thrombolytic therapy is necessary.

P2573 | BENCH
QT dynamics and microvolt T-wave alternans in patients with ventricular arrhythmias during exercise test

Purpose: It is important to study electrical instability markers in patients with idiopathic ventricular arrhythmias.
tricular arrhythmia (VA). A combination of non-invasive risk stratification markers for determining the presence of myocardial electrical instability is more actually. The best way is to reveal it during any modulation of the autonomic nervous system, such as physical exercise. In last years, much attention is paid to markers of changing repolarization - microtub 7-wave alternans (MTWA) and QT interval duration.

Objective: To study the dynamics of VA, MTWA, repolarization changes and the recovery heart rate (RHR) during exercise test in patients with idiopathic VA.

Materials and methods: 49 patients (26 men, mean age 43±12 years) with idiopathic VA (more than 300 per hour, day-long type). Structural cardiac pathology was excluded by ECG, echo and stress-echoCG, cardiac MRI. Exercise treadmill test (ETT) (protocol Bruse) was performed without any therapy, up to submaximal heart rate 85% or more. We studied MTWA, HR, VA, QT / QTC pre-test, peak and recovery period (ERP) during ETT.

Results: The volume of the achieved load was 10.6±2.4 and MET. HRR min was 26.5±9.5 bpm (normal). VA was in 66% patients - mean 6.3 single ventricular ectopic complexes (VE/min), at the peak ETT VA was in 44%, mean 3.4 VE/min. At rest, Q7 378.1+2.2 / QTC 433.5±19.9 ms, at the peak ETT Q7 326.7±7.4 / QTC 478.1±44.9 ms (p<0.05). QTC duration of more than 470 ms was in 61%, at ETT peak. MTWA was positive in 33.3% patients, and nine of them had an extending QTC, and other - normal. The probability of long QT syndrome diagnosis using diagnostic score is low in all the patients.

Conclusion: The probability of idiopathic VA is lower in 2nd-generation DES group compared with 1st-generation DES. The dynamic of VE during exercise test was not changed. The probability of idiopathic VA is lower in 2nd-generation DES group compared with 1st-generation DES.

**COMPLEX PCI**

P2575 | BEDSIDE

New-generation drug-eluting stents for unprotected left main coronary artery disease improve clinical outcomes?


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**Background:** About 5 years has passed since 2nd-generation drug-eluting-stent (DES) launched in Japan. Recent available data have shown the feasibility and the safety of new DES, but clinical outcomes data for left main coronary artery disease were scarce.

**Objective:** To evaluate the 1-year clinical outcomes in patients with unprotected left main coronary artery (ULMCA) disease treated with overall new DES options.

**Methods:** We analyzed retrospectively consecutive 2627 patients undergoing PCI angioplasty with sirolimus, paclitaxel, zotarolimus, (...) and everolimus-eluting stents from October 2008 to December 2013 in our hospital. A total of 151 patients with symptomatic coronary artery disease underwent angioplasty and were implanted some stents for de novo ULMCA lesions.

**Results:** Clinical follow-up was performed in 44 patients (95.4%) over a median of 295 days. There were no significant differences between two groups in lesion or patient characteristics, however procedure time was shorter in 2nd-generation DES group (136.9±77.1 min vs 103.9±56.5 min, P=0.001). The mean SYNTAX score was comparable in both group (25.8±11.0 vs 26.9±10.9, P=0.8), but the SYNTAX score was extremely lower in 2nd-generation DES group compared with 1st-generation DES group (1.8% vs 22.6%, P=0.01).

**Conclusions:** A good safety and efficacy profile has been shown with the use of 2nd-generation DES for the treatment of ULMCA disease, with a significant decrease in the need for repeat revascularization when compared to 1st-generation DES.

P2576 | BEDSIDE

Early vascular healing after titanium-nitride-oxide-coated stent vs. platinum chromium everolimus-eluting stent implantation in patients with acute coronary syndromes

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**Purpose:** Recent data suggests a paradigm shift in stent thrombosis (ST) occurrence as evidenced by lower rates of early and late ST in patients treated with platinum chromium everolimus-eluting stents (PtCr-EES) compared to traditional bare metal stents. Nevertheless, data on early vascular healing response of novel stent devices are scarce. In this randomized prospective trial, we sought to compare early healing and neointimal coverage of vessels treated with bioactive titanium-nitride-oxide-coated stents with thin strut platform (BAS) versus PtCr-EES at 2 months follow-up in patients with ACS.

**Methods:** Thirty-eight patients with ACS were randomized to receive either BAS (n=19) or PtCr-EES (n=19). Neointimal coverage and apposition was examined by OCT and intravascular coronary flow reserve measurement (CFR) at 2 months.

**Results:** At 63±8 days, 302 cross-sections (3412 struts) were analyzed in the BAS group, and 324 cross-sections (3460 struts) in the PtCr-EES group. Mean ± SD neointimal thickness was 240±127 μm and 65.4±59.5 μm for BAS and PtCr-EES, respectively (p=0.001). Median [IQR] percentage of uncovered struts was 1.2 [2.8] % vs. 11.3 [17.7] % (p<0.001). Median percentage of malapposed struts was 0 [1.20] % vs. 6.8 [3.59] % (p<0.026). CFR values between groups were comparable.

**Conclusions:** BAS showed rapid and comprehensive neointimal coverage at 2 months as compared to PtCr-EES, with significant neointimal hyperplasia. Furthermore, less strut malapposition was found in BAS.

P2577 | BEDSIDE

Mesh-covered stent implantation in addition to a distal embolic protection device leads to significantly higher velocity rates in highly degenerated bypass lesions

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**Background:** Percutaneous coronary intervention (PCI) for the treatment of aortoconary saphenous vein graft lesions (SVG) may include distal embolic protection devices (PED) to reduce atherothrombotic embolization. The potential benefit of the combination of a mesh-covered MGuard stent (MG) with a distal embolic protection device remains unknown.

**Methods:** This study analyzed 78 consecutive patients with SVG-PCI between 2010 and 2012 in four groups (conventional stenting (CS) vs. MGuard stent (MG) with or without PD). Only patients with a SVG degeneration score ≥1 were included. A post-procedural creatine kinase was assessed (CK, U/l). Graft dimensions were measured using quantitative coronary angiography. Adjusted TIMI frame counts were determined and estimated TIMI velocity rates (VE) were calculated accordingly (cm/sec).

**Results:** SVG degeneration score was 1.4±0.5 and significantly lower in grafts treated by CS (n=29) as compared to all other patients (1.8±0.8) treated with either PD (n=8), MG stents (n=28), or both (n=9), (p=0.01). CK release was lowest in MG stents including a PD (MG-PD: 142±77 vs. 440±1160, p=0.3). Also, post-procedure VE was significantly higher in the MG-PD group (7.1±7.2) as compared to the MG stent alone (11.8±5.1, p=0.02) or the conventional stent with or without PD (11.7±5.7, p=0.02).

**Conclusion:** The complementary application of a mesh-covered stent including a distal embolic protection device showed significantly higher TIMI velocity (VE) post PCI and a trend towards reduced CK release. This may be an appealing concept for a prospective randomized clinical trial in highly degenerated SVG lesions.
P2578 | BEDSIDE
Revascularization strategies for patients with multiple vessel disease and unprotected left main with a cobalt-chromium rapamycin eluting stent (ERACI IV Registry)

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Objectives: The primary endpoint of ERACI IV Registry was to assess the incidence of major adverse cardiovascular events (MACCE) in patients (pts) with coronary artery disease (CAD) using Firebird-2 (2nd generation rapamycin eluting stent) vs. ERACI III population (Drug eluting stent [DES] and bypass surgery [CABG] arms) at 30 days, 6 and 12 months of follow-up.

Methods: From March 2013 to February 2014, 225 pts with CAD undergoing DES implantation in 15 centers in Argentina were prospectively included. The registry was approved and monitored by an independent safety committee. Inclusion criteria were indication of myocardial revascularization and lesions ≥70% in ≥2 coronary arteries and/or unprotected left main disease. Exclusion were poor ejection fraction, recent STEMI (< 72 hours), previous PCI with DES, lesion diameter < 2.5 mm, renal failure and contraindications for dual antiplatelet therapy. MACCE was defined as any cause of death, myocardial infarction (MI), stroke or unplanned revascularization. Stent thrombosis was also analyzed. The only DES allowed was Firebird-2 (MicroPort Medical Shangai Co., Ltd), whereas in ERACI first DES generation was used.

Results: Baseline characteristics included age 63.8±11.1 years, 84.4% of males, 29.7% diabetes, 56% had unstable angina and 67.7% of pts 3 vessels or left main disease. 1.7±0.9 lesions treated per pts and 1.82 rapamycin eluting DES implanted. Procedural success was 100%. At discharge 100% received thienopodiprines (58.3% clopidogrel, 28.0% prasugrel and 13.7% ticagrelor). 30 days results are reported in Table.

Conclusions: 30 days ERACI IV registry showed a remarkable low incidence of MACCE in any of the components of the primary endpoint. Complete six months follow up will be available at the time of presentation.

P2579 | SPOTLIGHT
Long-term outcomes of optimal medical therapy versus percutaneous coronary intervention for patients with chronic coronary total occlusion

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Objectives: The primary endpoint of ERACI IV Registry was to assess the incidence of major adverse cardiovascular events (MACCE) in patients (pts) with coronary artery disease (CAD) using Firebird-2 (2nd generation rapamycin eluting stent) vs. ERACI III population (Drug eluting stent [DES] and bypass surgery [CABG] arms) at 30 days, 6 and 12 months of follow-up.

Methods: From March 2013 to February 2014, 225 pts with CAD undergoing DES implantation in 15 centers in Argentina were prospectively included. The registry was approved and monitored by an independent safety committee. Inclusion criteria were indication of myocardial revascularization and lesions ≥70% in ≥2 coronary arteries and/or unprotected left main disease. Exclusion were poor ejection fraction, recent STEMI (< 72 hours), previous PCI with DES, lesion diameter < 2.5 mm, renal failure and contraindications for dual antiplatelet therapy. MACCE was defined as any cause of death, myocardial infarction (MI), stroke or unplanned revascularization. Stent thrombosis was also analyzed. The only DES allowed was Firebird-2 (MicroPort Medical Shangai Co., Ltd), whereas in ERACI first DES generation was used.

Results: Baseline characteristics included age 63.8±11.1 years, 84.4% of males, 29.7% diabetes, 56% had unstable angina and 67.7% of pts 3 vessels or left main disease. 1.7±0.9 lesions treated per pts and 1.82 rapamycin eluting DES implanted. Procedural success was 100%. At discharge 100% received thienopodiprines (58.3% clopidogrel, 28.0% prasugrel and 13.7% ticagrelor). 30 days results are reported in Table.

Conclusions: 30 days ERACI IV registry showed a remarkable low incidence of MACCE in any of the components of the primary endpoint. Complete six months follow up will be available at the time of presentation.
dedicated operators can significantly enhance the chances of revascularisation of complex CTOs with a low risk of acute serious complications.

**P2581 | BEDSIDE**
Morphological characteristics of in-stent restenosis lesions after percutaneous coronary intervention for chronic total occlusive lesions assessed with optical coherence tomography

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**Background:** Little is known about morphological characteristics of in-stent restenosis (ISR) lesions after percutaneous coronary intervention (PCI) for chronic total occlusion (CTO) lesions.

**Methods:** Between June 2008 and January 2013, we performed optical coherence tomography (OCT) for 58 ISR lesions after PCI for CTO lesions and 150 after elective non-CTO lesions. We examined the difference between tissue morphologies of ISR lesions after CTO lesions and those after non-CTO lesions. The morphological assessment of neointimal tissue as to restenotic tissue structure, tissue backscatter, microvessels, lumen shape, and thrombus at the minimum lumen area site was performed.

**Results:** The results are shown in the figure.

**Conclusions:** The pathophysiology of ISR lesions after PCI for CTO lesions might be different from those after non-CTO lesions.

**P2582 | BEDSIDE**
Dedicated bifurcation BioSS® stent in the treatment of distal left main stem stenosis - International Registry

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**Purpose:** The aim of this study was to assess the effectiveness and safety profile of the distal LMS stent treatment with the dedicated stent bifurcation BioSS®: in subgroup I paclitaxel-eluting BioSS® Expert and in subgroup II sirolimus-eluting BioSS® LIM.

**Methods:** The enrollment of patients with coronary artery disease and NSTE-ACS was performed from radial access, and 83% with a 6F catheter. After 12 months in BioSS® Expert group angiographically driven TLR rate was pending - at 6 months there were no death or MI. Moreover, in BioSS® Expert group angiographic data disclosed that the late lumen loss was as following: in the main vessel - 0.21±0.1 mm, in the side branch – 0.26±0.12 mm and in the side branch – 0.14±0.09 mm.

**Conclusions:** Dedicated bifurcation BioSS® stents seem feasible devices with promising effectiveness and safety profile in distal LMS stenosis. Complete BioSS® LIM angiographic data will answer the question if the used drug is more important or maybe the stent design is crucial.

**P2583 | BEDSIDE**
Early healing profile of the new Dual Therapy EPC-Capturing Sirolimus DES; correlation of OCT coverage at 2 months to baseline CD34+, CD34+KDR+ cell tier: Subset analysis of the EGO-COMBO Study

S.W.L. Lee1, S.L. Kong1, E. Lichtenberg2, S.C.C. Lam1, K.K.W. Chan1, K.K.Y. Wu1, G.P. Shea , M. Haude3, R. Mehran4, A. Maehara5 on behalf of the EGO-COMBO Study Group, 1Queen Mary Hospital, Medicine (Cardiology), Hong Kong, Hong Kong SAR, People’s Republic of China; 2OrbusNeich Medical, Netherlands, Hoevelaken, Netherlands; 3Lukaskrankenhaus GmbH, Städtische Kliniken Neuss, Neuss, Germany; 4Mount Sinai School of Medicine, Zena and Michael A. Weiner Cardiovascular Institute, New York, United States of America; 5Columbia University Medical Center, Cardiovascular Research Foundation, New York, United States of America

**Background:** The Dual Therapy DES (EPC-capturing antibody & abluminal sirolimus coatings) is the first DES utilizing CD34+ antibody coating for rapid endothelialisation to enhance healing (measured by OCT % strut coverage). Using 4 sequential OCT FU baseline to 24M, the EGO-COMBO study is the first study ever designed to determine the healing profile of a DES. Correlations of the endothelial progenitor cell (EPC) tier with early strut coverage % were studied.

**Methods:** 61 patients treated by Dual Therapy DES received 4 sequential OCT FU baseline to 24M. EPC cell titres were analysed, using FACS analysis of fluorescent labeled blood samples for CD34, CD133 & KDR epitopes, and combinations thereof. EPC cell titres were analysed, using FACS analysis of fluorescent labeled blood samples for CD34, CD133 & KDR epitopes, and combinations thereof. Results: Using the best fit to a first order kinetics equation in the form y(t) = (1 - e^-ax), very early strut coverages (first patient group at 2nd month, n=12; 84.3% OCT coverage at 60 days) for this DES showed adequate correlation with baseline CD34+ cell titres (R2 = 58.9%) & slightly lower with CD34+/KDR+ (R2 = 47.8%). Correlations were largely absent for other epitopes and at later time points (n=49).

**Conclusions:** This subgroup analysis appeared to corroborate the effectiveness of CD34+ EPC capturing. Rapid early healing (84.3% strut coverage at 60 days) correlated positively with the baseline CD34+ & CD34+/KDR+ cell titres. Later (3-5 months) correlations were not found, likely because majority of stent struts had healed & were covered by 2 months.

**P2584 | BEDSIDE**
Which is best for pre-dilatation in biodegradable vascular scaffold implantation: non-compliant or compliant balloon?

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**Purpose:** Biodegradable Vascular Scaffold System (BVS) is the last generation fully absorbable vascular treatment system which is used for critical coronary stenoses. Despite its widespread use, technical and procedural details about BVS implantation is not very clear and need to be considered. In this study; we aim to compare the effectiveness of non-compliant balloon (NCB) and compliant balloon (CB) systems which are used for pre-dilatation before BVS implantation.

**Methods:** Sixty-eight (68) BVS procedures were analysed in the present study. Non-compliant balloon was performed to thirty-three (33) lesions and compliant balloon was performed to thirty-five (35) lesions. Two groups were compared to each other in terms of lesion properties and procedural features. Lesion
analysis was performed by quantitative coronary angiography (QCA) measurements. 

**Results:** There is no statistically significant difference between two groups in terms of lesion properties (reference vessel diameter, minimal lumen diameter, mean lesion length) before intervention.

Mean stent length and used opaque volume were similar between two groups. Procedure time and flouroscopy time were significantly lower in NCB group. Minimal lumen diameter after stent implantation was similar between groups (2.9±0.33 vs 2.8±0.25; p=0.36) but number of post dilasted lesions after stent implantation was significantly higher in CB group. (5 vs 14; p<0.03).

**Conclusions:** In conclusion; pre-dilatation with NCB before BVS implantation reduces the need for post dilatation. In addition use of NCB reduces the procedure time and flouroscopy time.

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**Table 1**

<table>
<thead>
<tr>
<th>All patients (N=108)</th>
<th>pDEB (N=52)</th>
<th>DES (N=56)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Non-fatal AMI</td>
<td>4 (3.7%)</td>
<td>2 (3.8%)</td>
<td>2 (3.6%)</td>
</tr>
<tr>
<td>TLR</td>
<td>10 (9.3%)</td>
<td>8 (15.4%)</td>
<td>2 (3.6%)</td>
</tr>
<tr>
<td>MACCE</td>
<td>13 (12%)</td>
<td>9 (17.3%)</td>
<td>4 (7.1%)</td>
</tr>
<tr>
<td>MB restenosis</td>
<td>8 (7.4%)</td>
<td>7 (13.5%)</td>
<td>1 (1.8%)</td>
</tr>
<tr>
<td>SB restenosis</td>
<td>5 (4.6%)</td>
<td>3 (5.8%)</td>
<td>2 (3.6%)</td>
</tr>
<tr>
<td>MB in-segment LLL (mm)</td>
<td>0.23±0.43</td>
<td>0.31±0.48</td>
<td>0.16±0.38</td>
</tr>
<tr>
<td>SB ostium LLL (mm)</td>
<td>−0.04±0.64</td>
<td>−0.04±0.76</td>
<td>−0.03±0.51</td>
</tr>
</tbody>
</table>

**Conclusions:** The strategy pDEB stent implantation with MACE showed better LLD than that in DES. Both strategies showed similar results on the SB.
P2589 | BEDSIDE
One-year clinical outcomes of total stent length after percutaneous coronary intervention with biolimus-eluting stent and everolimus-eluting stent
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Purpose: Total stent length (TSL) after first-generation drug-eluting stents (DES) implantation is associated with adverse cardiac events. However, it remains unclear whether TSL after newer-generation DES implantation has impacts on clinical outcomes. Our aim was to assess the relationship between TSL and clinical outcomes after the Nobori biolimus-eluting stent (BES) and the Xience/Promus everolimus-eluting stent (EES) implantation.

Methods: A total of 2272 patients with 3146 lesions undergoing BES (1270 patients with 1751 lesions) and EES (1002 patients with 1395 lesions) implantation between February 2010 and July 2012 were analyzed. Patients and Lesions were divided into quartile groups based on TSL. In BES group, TSL per patient (PA: 8 to 18 mm [n=341], LB: 19 to 24 mm [n=296], LC: 25 to 36 mm [n=365], PD: 57 to 220mm [n=268]), and TSL per lesion (LA: 8 to 18 mm [n=661], LB: 19 to 24 mm [n=294], LC: 24 to 38 mm [n=285], LD: 39 to 134 mm [n=253]). In EES group, TSL per patient (PA: 8 to 18 mm [n=253], LB: 19 to 23 mm [n=269], LC: 24 to 38 mm [n=258], LD: 39 to 130 mm [n=436]). In EES group, TSL per lesion (LA: 8 to 18 mm [n=624], LB: 19 to 24 mm [n=203], LC: 25 to 38 mm [n=360], LD: 39 to 130 mm [n=436]).

Results: In per-patient data, TSL per lesion (LA: 8 to 18 mm [n=661], LB: 19 to 24 mm [n=294], LC: 24 to 38 mm [n=285], LD: 39 to 134 mm [n=294]). In BES and EES groups, we assessed the year cumulative incidence of clinically driven target lesion revascularization (TLR) and definite stent thrombosis (ST) per patient and per lesion groupings, and cardiac death and myocardial infarction in the TSL per patient groups.

Conclusions: Longer TSL per lesion has significantly impacts on TLR rates in the BES group, whereas do not in the EES group. Longer TSL per lesion and patient is not associated with increased incidence of subacute and late as per academic research consortium definition) were identified. Detailed manual review of electronic medical records and review angiographic images were performed to identify patients with definite ST. Incidence of ST was significantly higher in the ABSORB™ (5.7% vs. 2.6%, P=0.001) and XIENCE™ (5.0% vs. 2.7%, P=0.001) groups compared to the BES group (0.9% vs. 2.7%, P=0.001). The incidence of MACE was also lower in the XIENCE™ group (3.4% vs. 10.0%, P=0.001), and target vessel revascularization (HR 0.77; 95% CI 0.59-1.00; p=0.05).

Results: In per-patient data, TSL per lesion (LA: 8 to 18 mm [n=661], LB: 19 to 24 mm [n=294], LC: 24 to 38 mm [n=285], LD: 39 to 134 mm [n=253]).

Conclusions: Longer TSL per lesion and patient is not associated with increased incidence of stent thrombosis through 1 year in the two groups.

P2590 | BEDSIDE
Impact of non-compliant balloon on long-term clinical outcomes in coronary bifurcation lesions: results from the COBIS (Coronary Bifurcation Stent) II registry
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Purpose: Non-compliant balloon (NCB) allows higher pressures without over- dilatation than compliant balloon (CB) in the case of side branch dilatation or kissing inflation, and may reduce side branch dissection or restenosis. We sought to investigate the impact of NCB on long-term clinical outcomes of patients receiving coronary bifurcation intervention.

Methods: From 18 major coronary intervention centers in our country, 2,897 consecutive patients were enrolled between January 2003 and December 2009. We compared major adverse cardiac events (MACE: cardiac death, myocardial infarction, or target lesion revascularization) between the NCB group (752 patients [26%]) and the CB group (2145 patients [74%]).

Results: NCB and CB were similarly used for left main bifurcations (30.9% vs. 29.0%, p=0.33) and true bifurcations (51.5% vs. 52.0%, p=0.81). In the NCB group, the two-stent strategy (30.9% vs. 25.1%, p=0.002), side branch predilation (40.6% vs. 31.2%, p=0.01), and final kissing balloon inflation (52.1% vs. 44.6%, p=0.001) were performed more frequently. The NCB group had a lower tendency in the rate of side branch occlusion during the procedure than did the CB group (6.2% vs. 7.7%, p=0.04). During median follow-up of 36 months, MACE occurred in 296 (10.2%) patients. The NCB group had a significantly lower MACE than the CB group (hazard ratio [HR] 0.67; 95% confidence interval [CI] 0.50-0.89; p=0.006). NCB was associated with a lower risk of death (HR 0.50; 95% CI 0.30-0.83; p=0.007), cardiac death (HR 0.17; 95% CI 0.05-0.57; p=0.004), the composite of cardiac death or myocardial infarction (HR 0.48; 95% CI 0.27-0.85; p=0.01), and target vessel revascularization (HR 0.77; 95% CI 0.59-1.00; p=0.05).

Clinical outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Non-compliant balloon (n=752)</th>
<th>Compliant balloon (n=2145)</th>
<th>p value</th>
<th>Adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>19 (2.5)</td>
<td>99 (4.6)</td>
<td>0.54 (0.33-0.87)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>3 (0.4)</td>
<td>39 (1.8)</td>
<td>0.21 (0.07-0.69)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiac death or MI</td>
<td>15 (2.0)</td>
<td>75 (3.5)</td>
<td>0.55 (0.32-0.96)</td>
<td>0.03</td>
</tr>
<tr>
<td>TLR</td>
<td>53 (7.0)</td>
<td>217 (9.8)</td>
<td>0.83 (0.61-1.13)</td>
<td>0.24</td>
</tr>
<tr>
<td>TVR</td>
<td>70 (10.0)</td>
<td>255 (11.5)</td>
<td>0.82 (0.63-1.06)</td>
<td>0.12</td>
</tr>
<tr>
<td>MACE</td>
<td>62 (8.2)</td>
<td>234 (10.9)</td>
<td>0.73 (0.57-0.97)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusions: The use of NCB is associated with favorable long-term clinical outcomes than CB in patients undergoing coronary bifurcation intervention.

P2591 | BEDSIDE
High density lipoprotein cholesterol and definite stent thrombosis

Background: Despite the use of dual antiplatelet therapy (DAPT), continued improvements in coronary stents and stent deployment; stent thrombosis (ST) remains a concern. Many characteristics including clinical, procedural and angiographic have been identified for ST. Low HDL-c is an independent predictor of acute platelet-dependent thrombus formation. We sought to study the role of HDL-c and ST.

Methods: We retrospectively examined percutaneous coronary intervention (PCI) database at our large academic center between 1/1/06 and 4/30/13. Patients with definite stent thrombosis within 1 year of index stent placement (acute, subacute and late as per academic research consortium definition) were identified. Detailed manual review of electronic medical records and review angiographic images were performed to identify patients with definite ST. Incidence of definite ST per 1000 person-months (p-m), clinical/lesion characteristics and procedural findings were compared between patients with low (< 40 mg/dl) or normal/high HDL-c (> 40 mg/dl) at index stent placement.

Results: A total of 8,385 patients with 10,547 cardiac catheterizations had stent placement during the study period. The study sample included 4075 patients who had a lipid profile reported within 3 months of index PCI. Of those, 49.4% had low HDL-c. 41.5% were male, 82.5% were caucasian, 28.2% had diabetes, 34.4% presented with STEMI as second anti-platelet agent. Out of 63 patients with ST, 47 (74.6%) didn’t have any definite identifiable cause of ST (interruption of DAPT or complication of primary stent placement). The rate of ST was slightly higher in patients with low HDL-c compared to those with normal/high HDL-c but the difference was not significant (1.5/1,000 p-m versus 1.12, p=0.22). Among patients with diabetes, ST was significantly higher in individuals with TSL < 40 cm (4.04% versus 2.6%, p=0.04) and rate of ST (p=0.05) in the EES group.

Conclusions: Diabetic patients with HDL-c < 40 have strong predisposition to definite ST. HDL functionality may be more important than HDL mass for its anti-thrombotic property. These initial observations would need to be confirmed in a larger patient population.
ond, p < 0.001). There were no significant differences in maximal inflation pressures and post-dilation-frequencies with non-compliant balloons between groups. Although device underexpansion was not significantly different, diameter-ratios was significantly higher in the BVS compared to the EES group, respectively (n=11 versus n=12, p = 1.000; 1.46 ± 0.20 versus 1.32 ± 0.19, p = 0.004).

Conclusion: Our data show, that local radial expansion is significantly reduced in BVS compared to EES. Although the clinical consequences of this finding are unclear, the reduced local radial expansion should be considered in the PCI strategy especially in calcified lesions.

P2593 | BEDSIDE
Impact of calcified plaque on stent strut distribution of bioresorbable vascular scaffolds versus metallic everolimus-eluting stents: an optical coherence tomography analysis

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Purpose: The aim of this study was to evaluate, using optical coherence tomography (OCT), the impact of underlying plaque morphology on strut distribution of bioresorbable vascular scaffolds (BVS 1.1) versus metallic everolimus eluting stents (EES).

Methods: Among 39 patients who underwent elective percutaneous coronary intervention (PCI) (n=20 in BVS group, n=19 in EES group), a total of 1200 post-PCI OCT frames (BVS: 590 frames; EES: 610 frames) were analyzed. Non-uniform strut distribution (NSD) was defined as a frame with maximum inter-strut angle >120°.

Results: The percentage of frames with NSD was significantly higher in the BVS group (26.1% [154/590] vs. 19.0% [116/610], p=0.003). In the EES group the arc of calcium was significantly greater than in frames with NSD as compared to those with USD (85.2°±62.6° vs. 21.0°±41.7°, p<0.01). On multivariable analysis, after adjustment for post-dilation balloon size and maximum inflation pressure, a calcium arc >75° was identified as an independent predictor of NSD after BVS implantation (odds ratio [OR]: 12.1, 95% confidence interval [CI]: 7.9-18.8, p<0.01).

Conclusions: The presence of calcified plaque behind BVS struts appears to be an independent predictor for NSD, particularly when the calcium arc exceeds 75°. For calcified lesions, meticulous lesion preparation, including use of dedicated devices, may help prevent NSD after BVS stent implantation.

P2594 | SPOTLIGHT
Bioresorbable vascular scaffold for coronary bifurcation lesions - results from the Real Absorb Registry

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Background: The use of Absorb Biodesorbable vascular scaffold (BVS) has largely been restricted to simple lesions with a relatively small experience in complex lesions. While it has been recommended to avoid BVS across side branch (SB) > 2.25 mm diameter, such bifurcations contribute nearly 25% of patients who undergo percutaneous coronary intervention (PCI). The strategies and results in such lesions yet remain undefined. We report the intermediate results of BVS in bifurcation lesions with SB > 2.25 mm (BL) from our Real Absorb Registry.

Methods and results: The “Real Absorb Registry” is a single centre registry of all Absorb BVS implanted in real life patients since its approval for unrestricted clinical use in December 2012 onwards. A total of 480 lesions in 365 patients were treated with 542 BVS. Among them 80 patients had 81 bifurcation lesions. The main bifurcation site was LAD/D1 in 77% (n=63). True bifurcation was found in 71% (n=58) of patients. Side branch (SB) was wired in 71% (n=58) and re-crossed in 43% (n=35). Pre-dilation and post-dilation of main branch (MB) was done in all patients. Provisional Stenting strategy was planned in 84% (n=68). Elective two BVS strategy was performed in 13 lesions (T stenting = 7, V stenting = 4 and T and micro protrusion TAP stenting = 2). Device and effective, with a high rate of procedural success and favourable short and long term outcome even in this very complex real world population
Conclusions: Although statistically significant differences in ST rates were observed between the different polymers and stent drugs, it was not possible to discriminate between the impact of polymer type or stent drug in the incidence of ST.

P2597 | BEDSIDE
Percutaneous treatment of coronary bifurcation: a network meta analysis of randomized controlled trial

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Purpose: The optimal percutaneous management of patients presenting with coronary bifurcation lesions remain to be defined.

Methods: Randomized controlled trial (RCT) comparing different treatments for bifurcation lesions were included. Major Adverse Cardiovascular Events (MACE, a composite end point of death, myocardial infarction, target lesion revascularization [TLR]) was the primary endpoint, while each single event of the MACE composite endpoint was evaluated separately as Stent Thrombosis (ST). Main analysis included studies evaluating different kind of treatment (provisional, T stenting, crush, culotte and double kissing double crush, DK crush) along with type of implanted stents (BMS, sirolimus and paclitaxel stents defined as first generation DES and Everolimus Eluting Stent [EES]) with or without final kissing balloon (FKB).

Results: Provisional strategy was evaluated in eleven studies with first generation DES and FKB (1819 patients) and without FKB in one RCT between 04/2003 to 05/2012. CR was achieved in 41% of the patients, and 61% of the lesions were IVUS guided. CR group was associated with lower rates of death/Q-MI at 1 year (adjusted HR: 0.695; CI: 0.4-0.9; P=0.048). Freedom from TLR and TLR was lower in CR vs. IR group (89% vs. 93%; Log Rank P-0.001) and (91% vs. 95%; Log Rank P-0.001). Stent thrombosis rates tended to be lower in the CR group (0.3% vs. 1.0%; P=0.074). IVUS independent the freedom from TLR in both CR (93% vs. 87%; Log Rank P=0.041) and IR (96% vs. 93%; Log Rank P-0.010) groups.

Conclusions: CR reduces the rates of death/Q-MI at 1 year with a cost of higher rates of repeat revascularization compared to IR. IVUS-guided PCI improves outcomes irrespective of the completeness of revascularization strategy. Our study suggests that CR with IVUS guidance is viable strategy to treat multi-vessel patients in the DES era.

ACUTE MYOCARDIAL INFARCTION AND PCI

P2600 | SPOTLIGHT
Long-term mortality of patients with ST-segment elevation versus non-ST-segment elevation myocardial infarction in the drug-eluting stent era: 5-year results of a large real-world registry

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Background: Difference in long-term mortality between ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI) have been demonstrated in a few studies. It remains unclear in the drug-eluting stent (DES) era.

Methods: We consecutively enrolled acute myocardial infarction (AMI) patients who underwent percutaneous coronary intervention (PCI) in the COREA-AMI (Convergent Registry of cardiac and chnnAm university for AMI) from January 2004 to December 2009. Of 4,748 AMI patients, 2,607 and 1,617 patients who treated with only DES were diagnosed with STEMI and NSTEMI, respectively. The primary endpoint is 30-day all-cause mortality and mortality from 31 days to 5 years. We performed landmark analysis at 30 days.

Results: Median follow up duration was 43.3 months (interquartile range 29.4 to 59.7 months). All-cause mortality rate at 30 days was higher in STEMI (3.6%; 94 patients) than NSTEMI (2.4%; 39 deaths; P=0.031). On the other hand, mortality from 31 days to 5 years was higher in NSTEMI (17.4% vs. 13.7%; 273 deaths vs. 343 deaths; P=0.001). After adjustment with clinical and angiographic characteristics, STEMI is associated with 30-day mortality (hazard ratio (HR) 1.54, 95% confidence interval (CI) 1.06-2.25, P=0.025) and NSTEMI is independent predictor for mortality from 31 days to 5 years (HR 1.28, 95% CI 1.07-1.48, P=0.006).

Conclusion: STEMI was associated with a higher risk of short-term mortality, but NSTEMI was associated with a higher risk of long-term mortality in the DES era.

P2601 | BEDSIDE
Early versus delayed percutaneous coronary intervention in patients with non-ST elevation acute coronary syndromes

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Introduction: International guidelines advocate early angiography and percutaneous coronary intervention (PCI) for high-risk patients presenting with non-ST elevation acute coronary syndromes (NSTEACS). Scoring systems, particularly GRACE and TIMI scores, have been used in clinical trials to identify high-risk patients. In real-world practice, the use of these scoring systems to guide timing of intervention appears to be limited. Thus it is unclear which patients are more likely to receive early PCI and how this impacts on short and long term clinical outcomes.

Objectives: The aim of this study is to compare the clinical characteristics and outcomes, both 30-day and 12 month, of patients with NSTEACS depending on the timing of their PCI from initial presentation.
Methods: The Melbourne Interventional Group Registry was analysed from 1st January 2005 until December 31st 2011. Patients who underwent PCI within a calendar day of presentation were included in the early PCI group. The delayed PCI group included all patients receiving intervention after one calendar day, but within the index admission. Patients transferred from a non-PCI capable hospital were excluded. Clinical characteristics and outcomes were obtained. The primary efficacy end points were 30-day and 12-month mortality, myocardial infarction (MI), target vessel revascularization (TVR) and major adverse cardiovascular events (MACE). The primary safety endpoint was in-hospital bleeding complications.

Results: 4307 patients with NSTEACS were included in the analysis with 51% undergoing PCI within a calendar day of admission. Patients undergoing delayed PCI were more likely to be older (67yrs vs 64yrs, p<0.01), have troponin elevation (70% vs 66%, p<0.01), have diabetes (32% vs 25%, p<0.01), have had a previous MI (33% vs 26%, p<0.01) and previous CAGS (14% vs 8%, p<0.01). Delayed PCI was associated with higher 12-month mortality (5% vs 3%, p<0.03), MI (8% vs 5%, p<0.01) and MACE (15% vs 12%, p<0.01). On multivariate analysis, delayed PCI was not an independent predictor of mortality at 12-months with an odds ratio of 0.95 (95% confidence interval, 0.68-1.31).

Conclusions: In an Australian PCI cohort, patients with NSTEACS and high risk features were more likely to undergo delayed PCI. Delayed PCI was not an independent predictor of mortality at 12-month outcomes.

P2602 | BEDSIDE
Short- and long-term outcomes after PCI for young patients with STE- and non STE-myocardial infarction
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It is well known that ST-elevation myocardial infarction (STEMI) is associated with an impaired acute prognosis, and early invasive management is recommended. However, the prognosis in patients 45 years or younger has not been well characterized.

Methods: We included consecutive STEMI patients from 2003-2012 (68,101 patient-years follow-up) who were treated in Eastern Denmark and Southern Sweden with percutaneous coronary intervention (PCI). We included 16,776 consecutive patients from the Eastern Danish Heart Registry and the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Short- and long-term mortality between young (<45) and older (>45) STEMI patients was compared.

Results: We identified 1036 (6.2%) patients up to 45 years of age (mean age 40.7 vs. 66.2 years, p<0.001). Patients in the young group were predominantly men (79.7% vs. 71.2%) and smokers (71.3% vs. 44.2%, p<0.001) but with a lower prevalence of hypertension (17.3% vs. 39.9%), hyperlipidemia (18.2% vs. 24.1%), diabetes (8.9% vs. 12.5%) and previous myocardial infarction (7.0% vs. 12.6%, p<0.001) compared to older patients. Young patients had a 0.8% annual mortality (Figure). Both, 30-day-mortality (adjusted hazard ratio [HR] = 0.29, CI 0.15–0.57, p<0.001) and mortality after 30 days and onwards (HR=0.22, CI 0.14–0.33, p<0.001) was significantly lower in the young group.

Conclusions: STEMI patients, age 45 years or younger, treated with primary PCI have an excellent prognosis after treatment with primary PCI. Long term annual survival is more than 99% in these patients.

P2603 | BEDSIDE
Association between hospital characteristics, missed care opportunities and mortality in patients with STEMI. A cohort study on STEMI epidemiology and outcomes in Eastern Denmark.
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1 Rigshospitalet - Copenhagen University Hospital, Heart Centre, Copenhagen, Denmark; 2 Skane University Hospital, Department of Cardiology, Lund, Sweden; 3 Uppsala University Hospital, Department of Medical Sciences, Cardiology, and Upplands Cardiovascular Research Centre, Uppsala, Sweden; 4 Glostrup Hospital, Department of Internal Medicine, Section of Cardiology, Glostrup, Denmark

It is well known that STEMI is associated with a high risk of acute complications, and early invasive management is recommended. However, the prognosis in patients 45 years or younger has not been well characterized.

Methods: We included consecutive STEMI patients from 2003-2012 (68,101 patient-years follow-up) who were treated in Eastern Denmark and Southern Sweden with percutaneous coronary intervention (PCI). We included 16,776 consecutive patients from the Eastern Danish Heart Registry and the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). Short- and long-term mortality between young (<45) and older (>45) STEMI patients was compared.

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P2604 | BEDSIDE
The time of cardiovascular adverse events onset in patients with acute myocardial infarction after successful revascularization is independently predicted by proteolysis activity level
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Background: Blood flow restoration after myocardial revascularization does not eliminate further atherosclerosis progression, microcirculation changes, acute and chronic postinfarction remodeling. All these processes include matrix degradation and restructuring. The objective of this study was to determine the proteolysis indexes, such as matrix metalloproteinases (MMP) activity and tissue inhibitors of MMP (TIMP), impact on the further course of the disease in patients (pts) with acute ST – elevation myocardial infarction (STEMI) after successful revascularization.

Methods: We investigated the successive changes of intracoronary and venous serum MMP, MMP activity (gelatin-zymography; referent value–100% from normal subject plasma pool) and their interrelation, TIMP1 levels in 384 samples from 64 pts with STEMI before and after successful PCI, at discharge (7th day). Follow-up was approximately 1.5 years. ROC analysis, Spearman correlation analysis were used to test the statistical significance of the differences among the calculated index values.

Results: In all patients the occurrence of early main adverse cardiovascular events was significantly associated with high TIMP1 level, >116 ng/ml (AUC = 0.63±0.09; p=0.0005) in systemic blood, MMP2 activity level >100% in coronary arteries (AUC = 0.67±0.07; p=0.005) before revascularization and MMP2 activity level >100% in systemic blood (AUC = 0.93±0.05; p<0.003) before revascularization. For all indexes sensitivity ranged from 60% to 88%, specificity from 49% to 97%. For the first time it was revealed that a moderate increase of MMP2 activity level in systemic blood in 7 days after revascularization was associated with the later cardiovascular adverse events occurrence (p<0.0002), while in patients with TIMP1 additional determination of MMP2 and MMP9 systemic blood activity and MMP9/MMP2 activity interrelation on 7-th day after revascularization is recommended in order to predict the time of main adverse cardiovascular events occurrence even after successful revascularization thereby promptly identify patients subgroup for prolonged aggressive medical therapy.

Conclusion: For STEMI, there was a significant association between hospital missed opportunity for care, hospital facilities and early but not later mortality. Hospitals with fewer missed opportunities for care more frequently had PCI facilities and were higher volume centres.
P2607 | BEDSIDE
Risk assessment of complete left bundle branch block based on left ventricular ejection fraction for sudden cardiac death in myocardial infarction patients


Purpose: Low ejection fraction (EF) is a risk factor of sudden cardiac death (SCD) in myocardial infarction (MI) patients; however, the impact of complete left bundle branch block (CLBBB) on SCD is unclear. Thus, we examined the relationship between CLBBB and SCD based on EF.

Methods: A total of 1346 patients underwent sirolimus-eluting stent (SES) implantation for old MI or acute MI from 2002 to 2007, 937 of whom underwent thrombolysis or left ventriculography or electrocardiography after 8 months and were categorized into three groups according to EF: normal, >55%; low, 35-55%; and very low, <35%. The incidence of SCD was compared between CLBBB and non-CLBBB based on EF.

Results: The median follow-up time of the 937 patients was 2251 days. A total of 28 SCD occurred and the table shows the ratio of SCD between CLBBB and non-CLBBB based on EF.

The incidence of SCD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All EF &gt;55%</th>
<th>EF 35-55%</th>
<th>EF &lt;35%</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>28/937 (3.0%)</td>
<td>3/410 (0.7%)</td>
<td>17/466 (3.7%)</td>
</tr>
<tr>
<td>Non-CLBBB</td>
<td>22/896 (2.5%)</td>
<td>3/405 (0.7%)</td>
<td>16/431 (3.7%)</td>
</tr>
<tr>
<td>CLBBB</td>
<td>6/41 (14.6%)</td>
<td>0.5 (0.1%)</td>
<td>2/5 (4%)</td>
</tr>
</tbody>
</table>

P<0.0016.

Conclusions: In MI patients after SES implantation, CLBBB patients with EF <35% may be a risk factor of SCD.

P2608 | BEDSIDE
Impact of transradial approach on long-term mortality after PCI in real-life population

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Background: The rate of transradial approach (TRA) to PCI is increasing worldwide but there is still conflicting data regarding its impact on mortality. Purpose of this study was to compare the mortality after TRA versus transfemoral approach (TFA) PCI in large cohort of consecutive patients within the nationwide, real-life registry.

Methodology: The statistical analysis was based on first PCI procedure via TRA (N=2245) and TFA (N=75,325) collected in the Czech National PCI Registry between January 2005 and June 2011. After adjustment for sex, age, body-mass index, PCI indication, ejection fraction, left anterior descending artery as target vessel and Killip class for STEMI only, the balanced dataset was matched 1:2 (N=43,460) (average age 65±11). The long-term mortality up to 6 years was assessed independently from the operators. Three main groups of patients were identified based on their primary diagnoses: ACS without/with ST elevations (STEMI; NSTE) and stable CAD.

Results: The use of TRA was associated with significant decrease of long-term mortality.

Cumulative incidence was estimated by the Kaplan-Meier method. Unadjusted and adjusted HR and 95% CI were estimated by the Cox proportional hazard models.
mortality in patients with ACS, both with STEMI and NSTE. This difference was specifically observed during the 30-day follow-up (Table 1).

Conclusion: In real-life practice, the TRA PCI was associated with significant long-term decrease of mortality in patients with ACS (both STEMI and NSTE). This difference was particularly observed during the 30-day follow-up. No difference was observed in patients with stable CAD.

P2610 | BENCH
Drug eluting stents in female diabetic patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (PCI) in female patient with acute myocardial infarction (AMI) and diabetes mellitus (DM).

Methods: We selected 1799 consecutive AMI female patients (88.9±10.2) with DM undergoing primary PCI and divided them into 5 groups based on the types of drug eluting stents implanted. Sirolimus-eluting stent (SES), Paclitaxel-eluting stent (PES), Zotarolimus-eluting stent (ZES), Everolimus-eluting stent (EES), Biolimus-eluting stent (BES), Zotarolimus-eluting stent (ZES). Study end point was 12-month adverse cardiac events (MACE), a composite of death, fatal and nonfatal myocardial infarction, cardiac death, and non cardiac death (NCD). We calculated the incidence of 12-month MACE in SES, PES, EES, BES, ZES.

Results: Mean Hemoglobin A1c level of SES, PES, EES, BES, ZES was 7.7±1.1%, 7.8±1.3%, 7.8±1.7%, 7.6±1.2%, and 7.7±1.2% respectively (p=0.195). 928 patients (51.6%) patients prescribed OHA and insulin both. Ejection fraction, systolic blood pressure were no significant difference in five groups. The incidence of 12-month MACE in SES, PES, EES, BES, ZES was 8.3%, 8.9%, 4.2%, 4.5%, and 5.2%, respectively (p=0.02). Kaplan Meier analysis show significant difference between SES and BES (p=0.046). SES and EES (p=0.02), PES and BES (p=0.021), PES and ZES (p=0.039), PES and BES (p=0.011). Independent predictors of one-year MACE were family history (OR 17.06, 95% CI 8.42-34.61, p<0.001), serum glucose level (OR 0.304, 95% CI 0.140-0.661, p=0.02), serum creatinine level (OR 1.31, 95% CI 1.194-1.432, p=0.034).

Conclusion: In female patient with AMI and DM, PES and BES would be better therapeutic option than SES and PES for one-year follow up and this result warranted further long-term follow-up.

P2611 | BEDSIDE
Real world comparison of MGuard stent versus bare metal stent for ST elevation myocardial infarction
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Purpose: To assess MGuard stent (MGS) safety and efficacy for STEMI in the real world and compared to bare metal stent (BMS).

Methods and results: 262 patients were included in a single center. In 35.9% MGS was implanted. After propensity score matching two equivalent groups for baseline preprocedure variables of 79 patients were established. The mean follow-up was 321±12.94 days. No differences were found in all-cause mortality (7.6% in both groups), MACE (20.3% vs. 12.7%; p=0.198) or non cardiac mortality and non fatal infarction (6.3% in both groups). TLR was significantly higher in MGS group (11.4% vs. 1.3% (p<0.01; RIR 10.02[1,23-81.16]). (Figure 1 and Table 1).

Table 1. Basal and periprocedural characteristics. Events during follow-up

MGS (n=79) BMS (n=79) p
Basal characteristics.
Age (years) 59.56 (18.6) 62.56 (17.4) 0.141
Gender (male%) 88.6 (68) 87.1 (74) 0.513
Hypertension (%) 46.8 (37) 40.5 (32) 0.423
Diabetes mellitus (%) 20.3 (16) 12.7 (10) 0.198
Hypercholesterolemia (%) 50.6 (40) 45.6 (36) 0.524
Smoking (%) 62.0 (49) 53.2 (42) 0.260
Infarct related artery (right coronary artery %) 55.7 (44) 64.6 (51) 0.213
Baseline TIMI flow (0%) 88.6 (70) 89.1 (68) 0.566
Post-stent TIMI flow (3%) 97.5 (77) 94.9 (75) 0.339
Thrombectomy 83.5 (66) 82.3 (65) 0.833
Total stent length (mm) 23.13±13.65 23.65±11.16 0.717
Maximal stent diameter (mm) 3.30±0.38 3.34±0.47 0.610

Events during follow-up
All cause mortality 7.6 (6) 7.6 (6) 1
MACE 20.3 (16) 12.7 (10) 0.198
Target lesion revascularization 11.4 (9) 1.3 (1) 0.009

Conclusion: Our study is the first to compare MGS with BMS for STEMI in the real world and seems to confirm that even though MGS is a safe device and doesn’t increase mortality, is linked to high rate of long-term TLR.
of 6 (4–8) years, the prevalence of MACEs was significantly different among the 3 groups (low, 11.6%; medium, 20.8%; high, 31.8%; P<0.0002) (Fig. 1). The multivariate analysis revealed that the residual CABG SYNTAX score (≥30) was associated with substantially low MACEs-free survival (hazard ratio: 1.80, 95% CI: 1.11-2.92, P<0.017) (Table).

Conclusions: The residual CABG SYNTAX score was shown to be a powerful prognostic indicator, and is useful tool for risk stratification for CABG patients undergoing PCI.

P2614 | BEDSIDE
Prognosis and disease progression in patients under 50 years old undergoing PCI: The CRAGS (Coronary aRtery disease in young adults) study

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Objective: Young patients undergoing percutaneous coronary intervention (PCI) are generally considered at low procedural risk, but the potentially aggressive nature of coronary artery disease and long expectancy of life expose them at high risk of recurrent coronary events. The extent and determinants of disease progression in this patient subset remain largely unknown. The aim of the present study was to evaluate general risk factors for late outcomes after PCI among patients <50 years old.

Approach: A multicenter European retrospective registry which enrolled 1617 patients (age <50 years) undergoing PCI between years 2002 to 2012. The median follow-up was 3.0 years.

Results: The majority of patients were smokers, but on adequate secondary prevention medication including statins, aspirin, beta-blockers and ACE-inhibitors/AT-blockers. At 5 years, survival was 97.8%, freedom from major adverse cardiac and cerebrovascular events 74.1%, from repeat revascularization 77.8% and from myocardial infarction 89.9%. Altogether 13.5% of patients had a disease progression as an indication for repeat revascularization. Other indications for repeat revascularization were restenosis (7.1%) and stent thrombosis (2.1%) at 5 years follow-up. Independent predictors of disease progression after PCI were multivessel disease, diabetes and hypertension.

Conclusion: PCI is associated with excellent survival in patients <50 years old. Nevertheless, every eighth patient underwent repeat revascularizations due to disease progression in the median follow-up of three years despite guideline-adherent medication undersecing the need for more effective secondary prevention than currently available. Disease progression caused nearly two more ischemic recurrences than restenosis.

P2615 | BEDSIDE
The efficacy of second-generation drug-eluting stent for the treatment of left main and/or three vessel disease: propensity matched analysis

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Background: The efficacy of second-generation drug-eluting stent for the treatment of left main disease (LM) and/or three vessel disease (3V3D) remains unclear.

Methods: Between April 2008 and January 2013, 326 patients with LM and/or 3V3D were treated by percutaneous coronary intervention in our institution. In these patients, 154 patients were treated with first-generation DES and 137 patients were treated with second-generation DES. There were some differences in baseline characteristics between two groups, so we performed propensity matching to minimize the impact of confounding factors. Target lesion revascularization (TLR) and major adverse cardiac events (MACE) were compared between the two groups at 3 years.

Results: After propensity matching, there were 101 patients in each group. In the propensity matched cohort, incidence of TLR and MACE at 3 years were higher in first-generation DES compared with second-generation DES (TLR: 23.8% vs. 7.9%; P<0.003, MACE: 31.7% vs. 12.9%; P<0.002). Regarding the analysis stratified by the SYNTAX score, incidence of TLR and MACE in low and intermediate SYNTAX scores were tend to be high in first-generation DES group but there were no statistical significance (low score, TLR: 14.6% vs. 5.9%; P=0.258, MACE: 18.8% vs. 11.8%; P=0.481, intermediate score, TLR: 27.3% vs. 6.5%; P=0.116, MACE: 40.9% vs. 9.7%; P=0.052). On the other hand, in high SYNTAX scores the rates of TLR and MACE were significantly higher in first-generation DES group (TLR: 35.5% vs. 11.1%; P=0.020, MACE: 45.2% vs. 16.7%; P=0.048).

Conclusions: In propensity matched analysis, second-generation DES significantly improved TLR and MACE in patients with LM and/or 3V3D compared with first-generation DES.

P2616 | BEDSIDE
Analyses of long term mortality based on SYNTAX-Score and residual SYNTAX-Score in left main patients in acute setting
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Background: The SYNTAX-Score is a powerful indicator of long-term mortality in patients with left main coronary artery (LMCA) or multivessel disease undergoing percutaneous coronary intervention (PCI). The residual SYNTAX-Score (rSS), relating to the completeness of coronary revascularization, is a useful tool to predict long-term clinical outcome in PCI patients. However, the prognostic impact of these scores to predict 2 years survival after PCI for acute coronary syndrome involving the LMCA has not yet been demonstrated. We want to assess in patients with left main and multivessel disease correlation based on the SYNTAX score and long term mortality.

Methods: We retrospectively assessed long-term survival in 238 consecutive patients undergoing emergency PCI for acute coronary syndrome (i.e. STEMI or high-risk NSTEMI) from January 2005 to December 2011. All culprit lesions involved the LMCA, thus in all patients the LMCA was stented. We accurately reviewed the angiogram of all patients and calculated the SYNTAX-Score and the rSS, defined as the SYNTAX-score after PCI. The effect of reduction of SYNTAX-Score on all-cause mortality was assessed by dividing patients into tertiles of risk.

Results: 134 subjects underwent PCI for STEMI, and 104 for NSTEMI. Mean age was 67, mean SYNTAX and rSS score were 24. The mean follow-up was 2 years. Patients in the highest tertiles of risk score experienced a dramatically elevated mortality rate compared to the extremely low mortality rate in the lower tertiles. The ROC curve of survival and difference between SYNTAX-Score pre and residual SYNTAX-Score has been calculated. We used the Youden Index to identify a cut off value related to better survival and that was 13. We also analyzed the relation between the SYNTAX Score and the residual SYNTAX Score in the intermediate and high risk LMCA tertiles using chi square test. In patients with disease different than 13 survival was 54%. In patients with disease equal or more than 13 survival was 82%.9% (p-log value: 0.002).In patients with intermediate SYNTAX score the higher difference between SYNTAX pre and post is related to survival with odds ratio growing 0.85 related to delta SYNTAX (CI 1.03-1.20 p 0.007).

Conclusions: In our high risk LMCA patients the difference between SYNTAX score and residual SYNTAX score predicted a better outcome. A difference in SYNTAX/rSS equal or higher than 13 is related to better 2 years survival in intermediate tertile patients.

P2617 | BEDSIDE
Long-term prognostic value of deep spotty calcification for prediction of future revascularization: a prospective three-vessel intravascular ultrasound study
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Purpose: It is unclear what characteristics of plaque are associated with progression of stenosis in coronary arteries.

Methods: Consecutive 45 patients with coronary artery disease who underwent 3-vessel intravascular ultrasound (IVUS) examinations were prospectively enrolled in this study. Quantitative and qualitative IVUS analyses were performed for each non-significant non-culprit lesions. The maximum arc and the location (superficial or deep) of calcium were assessed at minimum lumen area (MLA). The longitudinal length of calcium was also measured. Quantitative analysis of plaque characterization was performed by scoring for echogenicity against the adventitia: brighter (hyperechogenic) or less bright (hypoechogenic), and the percentage of hyperechogenic plaque was calculated. The primary end point was the occurrence of non-culprit lesion-related revascularization (NCLR) during 6-years follow-up periods.

Results: A total of 163 non-significant non-culprit lesions with mild to moderate stenosis were identified on baseline 3-vessel IVUS. Of those 6 lesions of 6 patients required NCLR during follow-up periods. There were no significant difference in quantitative IVUS parameters including remodeling index and plaque burden between lesions with and without NCLR. Also, the percentage of hyperechogenic plaque in the lesion with NCLR was similar to that of the lesion without NCLR (35.3% vs. 34.1%, P=0.87). However, frequency of deep calcium with the maximum arc of <90° was significantly higher in lesions with NCLR than in lesions without NCLR (50.0% vs. 3.8%, P<0.002). The length of calcium was shorter and the maximum arc of calcium was significantly smaller in lesions with NCLR compared to lesions without NCLR (3.0mm vs. 5.9mm, P=0.07 and 46.7% vs. 117.8%, P=0.02, respectively).

Conclusions: A deep spotty calcium deposition on IVUS predicts the occurrence of revascularization for non-significant non-culprit lesions during 6-year follow-up periods. Spotty calcium may be a surrogate marker for plaque progression and subsequent revascularization in the future.

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P2618 | BEDSIDE
Periprocedural myocardial infarction predicts worse clinical outcome in patients undergoing percutaneous coronary interventions of chronic coronary total occlusion
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Purpose: Periprocedural myocardial infarction (PMI) after percutaneous coronary intervention (PCI) has been associated with higher mortality. PMI might occur more frequently during challenging procedures such as PCI of chronic coronary total occlusion (CTO). However, the prognostic implication of PMI in CTO-PCI remains unclear.

Methods: From January 2006 to September 2012, 715 consecutive patients (pts) undergoing PCI of CTO in major native coronary arteries were screened for this registry at 3 centers. Only pts with available pre- and post-PCI troponin (cTn) were finally included (n=442). PMI was defined as an elevation of cTn > 5 times URL in pts with normal baseline values or a rise of cTn > 20% if baseline values were elevated. Pts were grouped into: a) successful CTO-PCI and no-PMI (Group A, n=195); b) successful CTO-PCI with PMI (Group B, n=133); failed CTO-PCI (Group C, n=114). Major adverse cardiovascular events (MACE): composite of overall death plus non-fatal myocardial infarction plus target vessel revascularization) were assessed in 431 patients (97%) at a median follow-up of 25 months (10-37).

Results: The 3 groups did not differ significantly with respect to clinical characteristics. MACE rate was significantly lower in pts treated with successful CTO-PCI without PMI, and progressively increased in case of PMI or failed CTO-PCI (Group A vs Group B, 15%, Group C= 28%, HR: 1.57 (1.24-2.18), p<0.01). MACE-free survival was also significantly higher in Group A at Kaplan-Mayer analysis (Log-Rank: 7.17, p<0.01).

Conclusions: Occurrence of PMI during PCI of CTO is associated with worse clinical outcome, yet superior to patients with failed CTO recanalization.

P2620 | BEDSIDE
Coronary artery bypass graft surgery versus percutaneous coronary intervention for the treatment of unprotected left main coronary artery disease: a real world study with propensity score matching
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Purpose: Current guidelines recommend coronary artery bypass graft (CABG) surgery for the treatment of unprotected left main coronary artery (ULMCA) stenosis, although percutaneous coronary intervention (PCI) has recently proven to be an alternative in selected patients. The aim of our study was to compare the long-term outcomes of CABG versus PCI in the treatment of ULMCA disease.

Methods: We retrospectively studied 352 patients (88.4±10.2 years) with ULMCA disease undergoing CABG (n=307) or PCI (n=45) between January 2009 and June 2013. After matching by propensity score (n=68), we analysed the baseline characteristics of the sample and the rate of events. We performed a multivariate Cox regression model to predict the probability of major adverse cardiovascular and cerebrovascular events (MACCE) and a survival analysis with the Kaplan-Meier method.

Results: Mean follow-up was 888±470 days. The PCI group had a higher rate of MACCE (32.4% vs 11.8%, p<0.05) and a trend to more reinfarction and new revascularization. There were no differences in mortality between the two groups. Only a EUROSCORE II over 6 (HR 3.019, 95% CI 1.050 to 8.679, p=0.04) and conducting CABG (HR 0.247, 95% CI 0.076 to 0.801, p=0.02) were independent predictors of MACCE. In survival analysis, PCI group had an inferior MACCE-free survival (Log Rank 5.922, p=0.015) and Reinfarction-free survival (Log Rank 4.182, p=0.041) compared with CAGB group, with a tendency to inferior New Revascularizations-free survival (see Figure).

Conclusions: Despite the advances of PCI in recent years, CABG had better long-term outcomes in the treatment of ULMCA disease, especially at the expense of lower rate of reinfarction and new revascularizations.

P2619 | BEDSIDE
Value of SYNTAX score to predict long-term outcomes in patients undergoing percutaneous coronary intervention
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Purpose: The SYNTAX score (SS) is useful to quantify the extent of coronary artery disease (CAD) based on the location and complexity of each lesion. To investigate the association among clinical outcomes and value of the SS in patients undergoing percutaneous coronary intervention (PCI) with CAD. And to evaluate whether the SS is a predictor of long-term cardiovascular outcomes in patients treated with PCI.

Methods: A cohort of 1701 patients (69.7±10.7 years old, 77% male) who underwent PCI for CAD was analyzed from ICAS (Ibaraki Cardiovascular Assessment Study) multi-center registry between April 2007 to April 2010. We divided patients into 4 groups according to value of SS; Low SS (n=905), Intermediate SS (mid SS; 10-19: n=590), High SS (high SS; 20-26: n=191), and Very High SYNTAX (VH SS; 27-: n=176). Clinical outcomes were defined as Terminal events (TAR); death or myocardial infarction (MI). The incidence of heart failure or restenosis were no difference between four groups (CHF p=0.78, TLR p=0.94).

Results: Mean follow up period was 440 days. MACE was significantly higher in high SS than other three groups (Kruskal Wallis test p<0.05) and surprisingly there was remarkable different between high SS and very high SS. Similar significant difference was recognized between four groups in stroke and myocardial infarction (MI). The incidence of heart failure or restenosis were no difference between four groups (CHF p=0.78, TLR p=0.94).

Kaplan-Meier survival curves.

Conclusions: Despite the advances of PCI in recent years, CABG had better long-term outcomes in the treatment of ULMCA disease, especially at the expense of lower rate of reinfarction and new revascularizations.
TAX Score (RSS), which has been previously published, is determined as the SYNTAX score remaining after completion of PCI. We sought to assess its ability to stratify long-term outcomes in all patients who underwent PCI with sirolimus-eluting stents (SES).

Methods: Between August 2004 and March 2005, 218 patients were treated with SES at our institution. In the case of staged PCI procedure, the final planned procedure was used as the entry point for this study. Clinical follow-up was evaluated at more than 5 years. The RSS was available for 175 (80.2%) patients, except 43 patients with prior coronary artery bypass grafts surgery.

Results: Average follow-up period was 5.7±0.3 years. Patients were divided according to their RSS into tertiles defined as: RSS=0 (n=116), 0 < RSS-LOW ≤ 5 (n=27), RSS-HIGH > 5 (n=27). RSS-HIGH was significantly associated with a higher death rate (RSS=0: 18.1%, RSS-LOW: 22.3%, and RSS-HIGH: 41.6%; log-rank, P=0.030). Major adverse cardiovascular events (37.3%, 51.9%, and 78.9%, respectively; log-rank p=0.030). After multivariate analyses, independent predictors for major adverse cardiovascular events were the RSS (hazard ratio [HR]: 1.58, 95% confidence interval [CI]: 1.20 to 2.07; p=0.001), hemodialysis (HR: 2.62, 95% CI: 1.45 to 4.74; p=0.001), and age (HR: 1.02, 95% CI: 1.00 to 1.05; p=0.037).

Conclusion: The RSS is a useful score to predict the long-term outcomes in patients treated with SES in the real world setting.

P2624 | BEDSIDE
Comparison of one-year clinical outcomes in patients with diabetes mellitus after coronary intervention with biolimus- and everolimus-eluting stent
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Purpose: Recent pivotal trials have shown that biolimus-eluting stent (BES) is as safe and efficacious as everolimus-eluting stent (EES) with a durable bio-compatible polymer. However, the effectiveness of BES in a real-world setting of diabetic patients is currently unclear. We compared one-year clinical outcomes after the use of BES versus EES for the treatment of diabetic patients.

Method: We enrolled 1266 consecutive patients with the NOBORI BES, 563 after the use of BES versus EES for the treatment of diabetic patients. As a historical control group, a total of 1434 patients were treated with drug-eluting stent (DES). The primary endpoint was the rate of major adverse cardiovascular events (MACE), defined as a composite of cardiac death, non-fatal MI, and TLR. We compared the BES and EES groups.

Results: Baseline characteristics were similar between the BES and EES groups. At 1-year, the incidence of MACE was not significantly different between the BES and EES group (8.9% vs. 7.3%, P=0.28). Cumulative incidence of myocardial infarction, definite stent thrombosis, and clinically driven TLR were not significantly different between the 2 groups (1.0% vs. 0.9%, P=0.71, 0.9% vs. 0.9%, P=0.94; 7.3% vs. 4.7%, P=0.08, respectively). The incidence of TLR and Target vessel revascularization (TVR) was not significantly different between the 2 groups (11.9 vs. 11.6, P=0.58; 13.7% vs. 12.2%, P=0.40, respectively). The cumulative incidence of TLR was significantly lower in the BES group than in the SES and EES groups, both at 8 months and 20 months (Fig. 1). The cumulative incidence of TLR was significantly lower in the BES group than in the SES and EES groups (Fig. 2A). The cumulative incidence of MACE was also significantly lower in the BES group than in the SES and EES groups (Fig. 2B).

Conclusion: One-year clinical outcome after biodegradable polymer BES implantation in diabetic patients is not significantly different from that after durable polymer EES. This study suggests that both BES- and EES-use are acceptable in a real-world setting of diabetic patients.

P2626 | BEDSIDE
Syntex score-based assessment for stent failure among patients who underwent drug eluting stent implantation
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Background: Stent failure is the major determinant factor of prognosis among patients who underwent drug eluting stent (DES) implantation, and frequency of stent failure was increased with syntax score. However, detail of that interaction between stent failure and syntax score is still unclear.

Methods: Among total of 1286 patients who underwent PCI with DES, we investigated 1323 cases with DES failure. Stent failure was defined as angiographic restenosis or stent thrombosis. We divided them into three groups according to tertile of syntax score based on initial angiogram (low; 1-11, intermediate; 12-24, and high; >25), and compared pattern of stent failure and long-term outcomes among them. Stent fracture was assessed by fluoroscopy or IVUS in each case. Major adverse cardiac event was comprised from all cause death, non-fatal myocardial infarction, and re-target lesion revascularization (re-TLR).

Results: Among syntax score stratification, patients with DES failure was 29 cases in low, 39 cases in intermediate, and 55 cases in high syntax score tertile. Total stent length was increased with syntax score (mm; 30.1±19, 31.6±17, and 47.2±24; P=0.0003), and prevalence of overlapping stent was increased with syntax score (20.7%, 41.0%, and 67.3%, P=0.0001). Based on follow-up angiography, prevalence of focal restenosis was 75.0% of DES failure, and it was not different among those tertile. However, stent fracture was detected in 26.0% of DES failure, and it was frequently seen in patients with high syntax score (7.0%, 15.4%, and 43.6%, P=0.0002). Multivariate analysis revealed that syntax score (OR: 1.05, 95%CI: 1.02-1.09, P=0.003), over-lapping stent (OR: 0.90, 95%CI: 1.42-33.5, P=0.02) was independently related with occurrence of stent fracture. TLR including 2 cases of CABG was performed in all cases, but it was failed in 1 case. And survival analysis showed stent fracture was only independent predictor of occurrence of MACE among patients with DES failure (HR; 3.70, 95%CI; 1.20-11.3, P=0.02).

Conclusion: Among patients with DES failure, prevalence of stent fracture was increased with syntax score, and it was related to worse outcomes during subsequent follow-up periods. RCA lesion, overlapping stent, and complexity of coronary artery disease may influence on occurrence of stent fracture, and prevention of stent fracture might be key to improve outcomes among patients with high syntax score.

P2625 | BEDSIDE
Clinical and angiographic outcomes of full metal jacket stent implantation for right coronary artery: comparison between different drug-eluting stents
Purpose: Full metal jacket (FMJ) stent implantation has been used to treat diffuse coronary artery disease (CAD). However, the differences in outcomes after FMJ procedure between the implanted drug-eluting stent (DES) types were unknown. Thus, we evaluated clinical and angiographic outcomes after FMJ stent implantation for the right coronary artery (RCA) between sirolimus-eluting stent (SES), everolimus-eluting stent (EES), and biolimus-eluting stent (BES).

Methods: We defined FMJ as stenting without gaps from the ostium to the bifurcation of the RCA. The study population consisted of 166 consecutive patients who had been treated for de novo diffuse CAD with SES (77 patients), EES (60 patients) or BES (29 patients) from April 2004 to December 2012 in a single center. The patients who had 2 or more different DES types were excluded. Angiographic follow-up was routinely performed at 8 and 20 months after the procedure. Clinical outcomes were evaluated by major adverse cardiac events (MACE) and target lesion revascularization (TLR) at 2 years after the procedure. MACE was defined as a composite of cardiac death, non-fatal MI, and TLR. We compared the clinical and angiographic outcomes between patients based on the implanted stent types.

Results: The angiographic restenosis rate was significantly lower in the BES group than in the SES and EES groups, both at 8 months and 20 months (Fig. 1). The cumulative incidence of TLR was significantly lower in the BES group than in the SES and EES groups (Fig. 2A). The cumulative incidence of MACE was also significantly lower in the BES group than in the SES and EES groups (Fig. 2B).

Conclusion: In treating diffuse CAD requiring FMJ procedure, DES implantation was associated with more favorable outcomes compared with SES or EES implantation.
sions (CTO-PCI) can be increased by a retrograde approach. The impact of the retrograde compared to the antegrade PCI on long-term outcome is unknown.

**Aim of the study:** To evaluate the long-term MACCE rate (death, myocardial infarction, coronary bypass surgery and stroke) in patients after retrograde versus antegrade CTO-PCI.

**Methods and results:** In a prospective study from January 2008 to June 2012 436 consecutive patients with CTO’s (≥3 months old) were enrolled. Mean age was 63.4±10.3 years, 86% were male. The retrograde PCI, which was used only after a failed antegrade intervention, was performed in 18% (n=79) of patients. Procedural success with retrograde CTO-PCI had more frequently previous bypass surgery, RCA as target vessel (79.7% vs. 56.8%, p<0.0004), longer lesion length (46 vs. 30 mm, p<0.001), longer procedure duration (108.2 vs. 63.2 min, p<0.0001), higher contrast volume (433.6 vs. 267.6 ml, p<0.0001), longer fluoroscopy time (61.2 vs. 30.1 min, p<0.0001) and higher radiation exposure (285.3 vs. 145.0 Gy cm², p<0.0001).

Long-term overall MACCE rate (mean follow up 590±461 days) was not different after retrograde vs. antegrade CTO-PCI (14.3% vs. 15.1%). Same was true for the components of MACCE (death 5.7 vs. 8.5%, myocardial infarction 2.8 vs. 2.6%, bypass surgery 8.6 vs. 5.3%, stroke 0 vs. 2.6%).

However, patients with failed antegrade PCI had a significantly higher long-term MACCE rate compared to successful antegrade PCI (29.2 vs. 12.5%, p<0.04), whereas the MACCE rate of failed vs. successful retrograde PCI was not different (12.5 vs. 14.1%).

**Conclusions:** Despite more patients with previous coronary bypass surgery and more complex target lesions and procedures the overall long-term MACCE rate after retrograde CTO-PCI is not different to antegrade CTO-PCI. Why the long-term MACCE rate is higher only after failed vs. successful antegrade but not after failed vs. successful retrograde CTO-PCI deserves further studies.

**P2627 | BEDSIDE**

**Procedural and long-term outcomes in patients with chronic total occlusions treated by retrograde approach**

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**Purpose:** The retrograde approach has been developed to improve the procedural success in CTO lesions. However, little is known about how the retrograde procedure affects the long-term outcomes. We investigated the impact of the retrograde approach for chronic total occlusion (CTO) recanalization on procedural and long-term outcomes.

**Methods:** A total of 641 consecutive patients with 711 CTO lesions underwent percutaneous coronary intervention (PCI) at our institution between October 2005 and December 2008. The procedural and 5-year clinical outcomes were compared between 235 patients treated with the retrograde approach for at least 1 CTO and 406 patients treated with the antegrade approach alone.

**Results:** The procedural success rates were 80.9% and 92.9% (P<0.01). The retrograde CTO PCI was performed in 36.7% of patients. Coronary perforation including collateral channel injury was significantly more common in the retrograde CTO PCI than in the antegrade CTO PCI (15.7% vs. 5.7%, P<0.01). The median follow-up time was 5.3 years (interquartile range: 4.9 to 6.1 years). The cumulative incidence of cardiac death was similar in the 2 groups (5.8% vs. 5.7%, P=0.93). The cumulative 5-year incidence of revascularization for a vessel excluding target CTO vessel was similar between the 2 groups (61.3% vs. 59.5%, P=0.70). In the successful recanalization, the cumulative 5-year incidence of target vessel revascularization was similar between the 2 groups (34.9% vs. 30.2%, P=0.15). By multivariate analysis, procedural failure was an independent predictor of cardiac death (hazard ratio 2.84, 95% confidence interval 1.30 to 6.21, P<0.01).

**Conclusions:** The retrograde approach to support the successful recanalization is not significantly different compared with the conventional antegrade approach at long-term outcomes of patients with CTO undergoing PCI.

**P2628 | BEDSIDE**

**Predictors of successful chronic total occlusion (cto) revascularization- is there still a role for the old predictors?**

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**Background:** A chronic total occlusion (CTO) is one of the most technically challenging lesions for percutaneous coronary intervention (PCI). Only a small part of CTOs are intervened, perhaps because procedural success is limited by difficulties crossing and/or dilating the occluded segment. Improved techniques and the introduction of newer dedicated devices [wires, micro-catheters] have improved the success rate in crossing and treating CTO lesions.

**Aims:** We hypothesized that by using new tools and techniques, the known predictors of failure of CTO recanalization [heavy calcification, blunt/non-tapered occlusion, bridging collateral] become less significant. We thus aimed to analyze the factors that affect these predictors on success of recanalization.

**Methods:** We analyzed a total of 323 consecutive patients in whom CTO recanalization was attempted. We compared patient and angiographic characteristics between successful recanalization group (259 patients) and failed recanalization group (64 patients). CTO was defined as occlusion duration of >3 months or of unknown duration. Successful recanalization was defined as crossing a CTO lesion.

**Results:** Procedural success was observed in 80% of attempts.

**Conclusions:** Despite the use of dedicated wires, and new techniques of revascularization, the old predictors of failure of recanalization still played a role.

**P2629 | BEDSIDE**

**The factor of improvement of distal vessel diameter after percutaneous coronary intervention of chronic total occlusion in chronic phase**

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**Background:** Although the vessel diameter distal to the recanalized CTO lesion is often smaller than expected immediately after recanalization, the vessel tends to increase their diameter after one year. Therefore, we assessed how the distal segment vessel diameter would increase at 1-year follow-up.

**Methods:** Consecutive patients (n=104) who received successfully recanalization of CTO lesions from July 2007 to October 2011 and had 1-year follow-up catheterization were analyzed. We classified them into two groups by the Rentrop collateral flow grade: Group A, grade 0 to 2 and Group B, grade 3. We evaluated IVUS the plaque burden and minimum lumen diameter of the distal vessel segment immediately after recanalization. Vessel diameter distal to the recanalized CTO lesions (at 10mm from distal stent edge) was compared between follow-up and immediately after recanalization (baseline) by quantitative coronary angiography.

**Results:** Vessel diameter increased significantly from baseline to follow-up (1.9±0.7mm vs. 2.3±0.7mm, P<0.05). Vessel diameter increased more in Group B than in Group A (74.0% vs. 94.4% mm, P<0.05). There was no significant difference in IVUS findings between the patients with and without vessel diameter increase.

**Conclusion:** Vessel diameter in the distal segment of CTO lesion increased at 1-year follow-up especially in the patients with good collateral flow.

**P2630 | BEDSIDE**

**One-Year Clinical Outcomes with Biodegradable polymer Biolimus-Elluting stent in Chronic Total Occlusion: Comparison With Durable Polymer Everolimus-Elluting Stent**

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**Purpose:** Recent pivotal studies have shown that biolimus-elluting stent (BES) is as safe and efficacious as everolimus-elluting stent (EES). However, the effectiveness of BES in a real-world setting of chronic total occlusion (CTO) lesion is currently unclear. We compared one-year clinical outcomes after the use of BES versus EES for the treatment of CTO lesions.

**Method:** Between February 2011 and June 2012, we underwent percutaneous coronary intervention with the BES (1276 patients with 1752 lesions) or EES (1045 patients with 1446 lesions) were analyzed. Of these, 152 patients with 157 lesions and 137 patients with 142 lesions (9.9%) had CTO lesions. The primary endpoint was the cumulative rate of major adverse cardiac events, defined as a composite of cardiac death, myocardial infarction, definite stent thrombosis, clinically driven target lesion revascularization (TLR) at 1-year.

**Results:** Baseline characteristics were similar between the BES and EES groups. Total stent length did not differ between the 2 groups (52.8±26.5 mm vs. 52.7±30.1 mm, p=0.98). Diabetic patients and hemodialysis patients were similar.
between the 2 groups (46.5% vs. 44.3%, P=0.053; 3.2% vs. 2.8%, P=0.095, respectively). At 1-year, cumulative incidence of MACE and clinically driven TLRR were not significantly different between the 2 groups (4.5% vs. 3.5%, P=0.62; 3.8% vs. 2.8%, P=0.60, respectively). Stent thrombosis was similar between the BES and EES groups (0.6% vs. 0%, P=0.99).

Conclusions:: One-year clinical outcome after biodegradable polymer BES implantation in CTO lesions is not significantly different from that after durable polymer EES. This study suggests that both BES- and EES-use are feasible with efficacy and safety in a real-world setting of CTO lesion.

P2631 | BESDISE
Impact of calcium distribution for successful recanalization of coronary artery CTO: Assessment from computed tomography coronary angiography
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Purpose: The success rate of percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) is lower than overall success rate of other forms of PCI. Recent report suggested that severe calcified patterns at occluded segment by CT coronary angiography (CTCA) were prevalent in failed CTO. CTCA is potentially a useful imaging modality for characterization of CTO lesion. We aimed to investigate whether distribution of intramural calcification is related to wire penetration for occluded segment as observed CTCA.

Methods: We performed prospective observational study carried out in our institution between April 2007 and December 2013. We performed CTCA in a consecutive cohort of eligible patients who were scheduled for PCI of CTO. CTCA was performed with a 64-slice MSCT. The degree of calcification was evaluated by cross-sectional calcium images along the occluded segment. Further we analyzed the calcium spots which occupied at the occluded segment by cross-sectional lumen views. Intramural calcification (IC) was defined as the lesion which calcium spots occupied at the center of the lumen from cross-sectional lumen views, and Extramural calcification (EC) was defined as the lesion which calcium spots without the center of the lumen from cross-sectional lumen views. We compared with wire cross success rate and technical success rate between two groups.

Results: In a cohort of 256 patients with 286 CTO lesions were attempted. Two hundred and fifty-two of 286 (88.7%) CTO lesions were successfully revascularized with PCI. Of the 34 CTO lesions with failed PCI, 27 failed cases were due to failure of crossing the CTO lesions with angioplasty guidewires. Seven failed cases were due to failure of crossing the CTO lesions with the angioplasty balloon. Two hundred and eighty-six calcium calcified CTO lesions were divided into two groups: IC group (73 lesions) and EC group (213 lesions). Assessing from CTCA; either the frequency of calcification at the entry, calcification at the exit, length of occluded segment or calcium score of occluded segment were similar between two groups. Wire cross success rate in IC group was significantly higher than that of IC group (EC vs. IC: 94.8% vs. 49.3%, P=0.001). And technical success rate in IC group was significantly higher than that of IC group (EC vs. IC: 90.6% vs. 43.8%, P=0.001).

Conclusions: Intramural severe calcification has an impact on wire lesion crossed success rate during wire penetration for CTO. CTCA is the only modality to assess the occluded segment before PCI procedure and a possibility that procedural success can be predicted.

P2632 | BESDISE
Influence of stent length on long-term clinical outcomes after percutaneous coronary intervention for chronic total occlusions
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Purpose: Chronic coronary total occlusions (CTO) when successfully treated are often stented over very long sections. Studies have shown a correlation between stenting length and the occurrence of major adverse cardiac events (MACE) and its components, cardiac death, myocardial infarction (MI) and target vessel revascularization (TVR). Whether successful percutaneous coronary intervention (PCI) of a CTO is associated with improved long-term survival at up to 9 years. Successful PCI of CTO procedure.

Methods: Between 2004 and 2012, a total of 1,320 consecutive patients underwent PCI for CTO in our centre (14 operators). We compared cardiac death, target vessel revascularization (TVR), myocardial infarction (MI) and major adverse cardiac events (MACE) in patients with successful versus failed PCI at a mean follow up of 4.2 years (IQR: 2.5-7.0 years). Procedural success was defined as achievement of residual stenosis <50% with TIMI-3 flow in the target vessel.

Results: Successful treatment of CTO by PCI was achieved in 990/1320 (75.0%) patients. In patients with failed PCI, cardiac death occurred in 63.1±11 Vs. 65.4±11, respectively (P=0.01), had lower rates of hypertension (56.5% Vs. 66.9%, p<0.01), previous MI (19.4% Vs. 30.0% p<0.001), previous PCI (34.4% Vs. 42.1%, p<0.02), and previous CABG (5.5% Vs. 13.4%, p<0.001) than those in whom PCI success was not achieved. In addition, patients who achieved PCI success were more frequently treated for left anterior descending artery CTO (34.1% Vs. 22.1%, p<0.001) and had better baseline left ventricular ejection fraction (57.9% Vs. 55.9%, p<0.04), PCI success was associated with significantly lower rates of cardiac death (5.3% Vs. 11.7% for patients with failed PCI, p<0.001) and MACE (19.5% Vs. 26.3% respectively, p<0.001). Successful PCI (HR: 0.5; 95% CI: 0.32-0.81, p=0.005), diabetes (HR: 2.44; 95%CI: 1.52-3.83), left ventricular ejection fraction (per percent increment, HR: 0.96; 95% CI: 0.94-0.99, p<0.004) and age (per year increment, HR: 1.06; 95% CI: 1.03-1.08, p<0.001) were independent predictors of cardiac death at follow-up. There was a strong interaction between diabetes and procedural success or failure. Indeed, cardiac mortality rate was 4.1% (30/731 patients) after successful and 6.6% (15/227 patients) after failed PCI in non-diabetics, whereas it was 6.9% (18/259) and 19.4% (20/103) in diabetic patients, respectively (p<0.001).

Conclusions: In this large cohort of CTO-patients, successful PCI was associated with improved long-term survival at up to 9 years. Successful PCI of CTO is associated with superior cardiac death reduction among diabetic patients vs. non-diabetics, suggesting strong efforts to recanalize occluded coronary arteries in these patients.

P2634 | BESDISE
Regular drug eluting stent versus dedicated bifurcation BIOSM LIM stent in coronary bifurcation treatment - randomized POLBOS II study
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Purpose: POLBOS II study is the continuation of POLBOS I study (POLish Bi-furcation Optimising Strategy), in which paclitaxel-eluting stent BIOSM® Expert stent was compared with regular DES in the treatment of coronary bifurcations.

Methods: In POLBOS II study patients with stable coronary artery disease or NSTE-ACS who signed informed consent were randomized to the group where dedicated bifurcation sirolimus-eluting BIOSM® LIM stent was implanted or to the group where regular DES was used. The enrollment was proceeded between November 2012 and August 2013 in five centers in Poland and Spain. Patients with STEMI or Medina type 001 bifurcation lesions were excluded from the study. Provisional T-stenting was the obligatory strategy. An angiographic control was planned at 12 months in all patients. The primary end-point of the study is the rate of death, MI, ST and TLR after 12 months. Here, we present complete 6-month clinical follow-up. At the time of ESC Congress 2014 angiographic follow-up will be completed.

Results: In BIOSM® LIM was implanted in 85 patients (50.6%) and regular DES was deployed in 83 patients (49.4%). A fourth of participants were females. The average age of patients did not differ significantly between groups (BIOSM vs DES: 66.7 ± 65.5 yrs). In BIOSM group there were significantly more patients...
Conclusions: Collected data demonstrates comparable immediate and short-term clinical outcomes for both studied groups. Full data enable to answer the question if BioSS® LIM comparable to regular DES and if it is superior to BioSS® Expert stent assessed in POLBOS I study.

P2638 | BEDSIDE Preventive revascularization does not offer clinical advantage over a selective invasive strategy in patients with ST-segment elevation myocardial infarction and multivessel disease


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Purpose: The everolimus-eluting bioresorbable vascular scaffold has shown promising angiographic results and clinical outcomes in the context of first-in-man trials. However, more complex lesions, however, cannot be directly extrapolated from these data. We thus sought to evaluate the clinical impact of Absorb BVS on short-term outcomes in patients with more complex lesions in real-world clinical settings.

Methods: Since September 2012, Thoraxcenter commenced the ABSORB Expand single-arm registry using the Absorb BVS for patients with de novo complex lesions. We assessed bifurcation lesions treated with the Absorb BVS, involving a side branch (SB) >0.5mm, ostial lesion >40% stenosed, or a SB requiring pre-dilatation. Two-dimensional quantitative coronary angiography was performed with a dedicated bifurcation analysis algorithm and software. The primary endpoint was a device-oriented composite endpoint (DoCE) including cardiac death, myocardial infarction, and clinically driven target lesion revascularization.

Results: Consecutive 169 patients with 40 bifurcation lesions were studied. Mean age was 64 ± 7.4 years. Four patients presented with unstable angina and 13 patients were diagnosed as non-ST elevation myocardial infarction. Although 14 lesions (35.0%) revealed true bifurcation, 38 (95.0%) bifurcation lesions were treated by one-scaffold approach. Pre-procedure mean reference vessel diameter and diameter stenosis were 2.85 ± 0.45 mm and 80 ± 14%, respectively. Absorb BVS implantation did not alter the distal bifurcation angle (DMV-SB) pre- and post-procedurally (49.1 ± 9.4 vs. 45.4 degrees, p=0.11). In 16 lesions (40.0%), jailed polymeric struts were fenestrated at the ostium of SB. Although 2 lesions (5.0%) revealed SB occlusion immediately after Absorb BVS implantation, post-procedural TIMI flow grade 3 was achieved in all main vessels and SBs. Neither DoCE nor scaffold thrombosis were reported at 30 days follow-up.

Conclusions: The Absorb BVS appeared to be safe and feasible for the treatment of bifurcation lesions in real-world clinical settings.

PROGNOSTIC FACTORS IN ACUTE CORONARY SYNDROMES

P2637 | BEDSIDE Prognosis of non-ST elevation myocardial infarction in patients with high hemoglobin levels at admission

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Background: Previous studies have found that in patients with ST elevation myocardial infarction (STEMI) the presence of higher levels of hemoglobin (Hb) at baseline were associated with greater in-hospital mortality once reperfusion therapy may predispose to a prothrombotic state.

Objectives: We aim to assess whether in patients with non-ST elevation myocardial infarction (NSTEMI) higher Hb levels at admission are also associated with a worse prognosis when compared to individuals with the same diagnosis and lower Hb values.

Methods: 3793 consecutive patients with admission diagnosis of NSTEMI between 01/10/2010 and 01/10/2013 included in the database of a prospective national registry of acute coronary syndromes were analysed. 403 patients with no initial Hb levels evaluation were excluded. Patients were divided into 3 groups according to the values of Hb on admission: group 1 - Hb <12 g/dL; group 2 - Hb 12 and >16 g/dL, and group 3 - Hb >16 g/dL.

Results: 3396 patients entered the study of which 20.7% were included in group 1, 70.3% in group 2 and 9.1% in group 3. When compared with patients in group 2, the group with higher Hb levels had a higher proportion of males, patients were younger, were heavier, and had a higher body mass index (BMI), a higher % of smokers and lower GRACE score. Patients in group 1 were older, with higher GRACE score and higher creatinine values. The lower in-hospital mortality was observed in the group of subjects with Hb >16 g/dL (1.3%) whereas the mortality rate observed for patients with Hb ≤12 g/dL was about 4 times higher (5.4%, p=0.001). In multivariable analysis the value of Hb above 12 g/dL proved to be a protective factor compared with Hb <12 g/dL (OR 0.215, 95% CI 0.083-0.555).

Conclusion: Unlike observed in previous studies where higher Hb levels were associated with a worse prognosis in patients with STEMI, in this study it appears that in the context of NSTEMI increased values of Hb at admission are associated with a more favorable prognosis.

P2639 | BEDSIDE Early detection of cytochrome c in acute myocardial infarction identifies patients at higher risk of adverse outcomes

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Purpose: Cardiac troponins are commonly used as diagnostic and prognostic
buckmarks in patients with acute myocardial infarction (AMI), and for risk stratification to guide triage decisions and aid in treatment selection. In addition to sensitive markers of ischemic cell death, however, remains a need for new biomarkers of apoptotic cell death associated with myocardial reperfusion injury. Indeed, at the cellular level, reperfusion has been demonstrated to be a potent inducer of apoptosis through the activation of the mitochondrial pathway of apoptosis, release of apoptotic factors, including cytochrome c, to the cytosol where they activate the apoptotic cascade. Cytochrome c has been shown to transiently increase in the early phase of AMI, and its peak value to be associated with clinical, angiographic, and imaging variables of reperfusion. Despite these preliminary findings, support the concept that cytochrome c is a potential biomarker of myocardial reperfusion injury, no study has investigated, so far, the potential clinical and prognostic value of its early (at hospital presentation) measurement in AMI patients.

Methods: Serum cytochrome c (ELISA method) was measured at hospital admission in 753 consecutive patients with AMI (313 STEMI and 440 NSTEMI). In-hospital and 1-year mortalities were evaluated as primary end point. Results were analyzed according to the presence of positive or negative cytochrome c values at hospital admission.

Results: At hospital presentation, cytochrome c was detectable in the blood of 280 (37%) patients (positive group; median value 0.87 [0.63-1.29] ng/ml), whereas it was not detectable in the remaining 473 (63%) patients (negative group). The two groups were similar for all the evaluated variables, except for a lower rate of Killip class III-IV (76.9 vs 74.0%, P=0.74), however, by multivariate analysis the presence of AF wasn’t an independent predictor of in-hospital mortality. In-hospital and 1-year mortalities were evaluated as primary end point. Results were analyzed according to the presence of positive or negative cytochrome c values at hospital admission.

Conclusions: Cytochrome c positivity, as well as the extent of its rise, is closely associated with short- and long-term mortality.

P2640 | BEDSIDE

In-hospital clinical outcomes of the oldest-old patients with acute myocardial infarction treated with primary percutaneous coronary intervention

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Purpose: The aim of the present study was to assess the early clinical outcomes of the oldest-old patients (aged > or = 90 years) with acute ST-segment elevation myocardial infarction (STEMI) following primary percutaneous coronary intervention (PCI).

Methods: A total of 510 consecutive patients with acute STEMI who underwent primary PCI within 12 hours of symptom onset between January 2009 and December 2013 were enrolled. The in-hospital mortality was compared between oldest-old (26 patients, 5.1%, 92.7±3.0 years) and younger patients (71.7±13.4 years).

Results: There were no differences about the rate of TIMI 0-1 flow at presentation (76.9 vs 74.0%, P=0.74), use of stents (96.2 vs 95.0%, P=0.80), and the final rate of TIMI 3 flow (83.7 vs 84.3%, P=0.96) between the oldest-old group and the younger group. The overall in-hospital mortality was significantly higher in the oldest-old group than the younger group (26.9 vs 11.4%, P<0.001). When compared by baseline Killip class, the in-hospital mortality of the oldest-old was similar in the Killip class II (5.3 vs 2.9%, P=0.39), but was significantly higher in the Killip class III-IV (85.7 vs 42.3%, P<0.001). The final rate of TIMI 3 flow and the baseline Killip class III-IV were identified as independent predictors of the in-hospital mortality of the oldest-old patients.

Conclusion: STEMI patients with MVD at admission was associated with poor outcomes while in patients without HF no differences were observed irrespective of MVD. These findings could aid in the identification of patients that might benefit from preventive primary PCI.

P2642 | BEDSIDE

Atrial fibrillation during ST-elevation acute myocardial infarction: prevalence, predictors and impact in the treatment and mortality

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Purpose: To determine the incidence of the first episode of Atrial Fibrillation during hospitalization for STE elevation acute myocardial infarction (STEMI), to identify possible predictors of its onset and to assess its impact on therapy and in-hospital mortality.

Methods: We evaluated 3254 P with STEMI enrolled in a multicentre national registry. We considered two groups: P with AF and P without AF. We recorded age, gender, cardiovascular and non-cardiovascular co-morbidities, results of coronary angiography, number of angioplasties performed, in-hospital and at discharge therapy. We evaluated left ventricular ejection fraction (EF) and the presence of the following complications: heart failure (HF), need for mechanical ventilation, stroke, major bleeding and high grade atrio-ventricular block. We compared the in-hospital mortality and performed multivariate analysis to identify predictors of the incidence of AF and to assess the impact of AF in hospital mortality.

Results: The incidence of AF in STEMI was found in 15.4% of patients. Patients with AF were older (71.1±12 vs 62.1±14 years, p<0.001), more females (34.5% vs 24.4%, p<0.002), had higher prevalence of hypertension (72.4% vs 59.6%, p<0.001), valvular heart disease (3.7% vs 1.1%, p=0.008), previous HF (5.6% vs 1.8%, p=0.002) and chronic renal failure (6.2% vs 2.8%, p=0.007). There were no differences in the number and type of vessels with disease. Patients with AF received more therapy during hospitalization and at discharge with vitamin K antagonists (7.7% vs 1.5% and 12.3% vs 2.5%, p<0.001), loop diuretics (59.4% vs 24.3% and 51.3% vs 19.3%, p<0.001), aldosterone antagonists (27.0% vs 12.0% and 25.0% vs 11.1%, p<0.001), amiodarone (37.4% vs 4.1% and 37.4% vs 1.6%, p<0.001) and digoxin (10.2% vs 0.3% and 2.6% vs 0.3%, p<0.05). AF was associated with worse EF (p<0.001), higher prevalence of worsening HF (46.2% vs 16.2%, p<0.001), need for mechanical ventilation (10.7% vs 3.4%, p<0.001), stroke (24.6% vs 0.8%, p<0.001), high grade atrio-ventricular block (12.7% vs 5.4%, p<0.001) and major bleeding (6.1% vs 1.8%, p<0.001). In-hospital mortality was higher in P with AF (13.7% vs 4.6%, p<0.001), however, by multivariate analysis the presence of AF wasn’t an independent predictor of in-hospital mor-
tality. There were identified as independent predictors of AF: age and previous history of HF.

Conclusions: In our population of P with STEMI, the incidence of AF was 6.1% and is associated with an increased prevalence of in-hospital complications and mortality. The age and previous history of HF were identified as independent predictors of AF.

P2643 | BEDSIDE

Gender and age effects on in-hospital mortality of ST-elevation myocardial infarction: a nationwide registry study

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Purpose: Previous studies have suggested that women may have higher mortality than men after myocardial infarction. We studied gender and age differences in in-hospital mortality of ST-elevation myocardial infarction (STEMI).

Methods: In-hospital mortality of all STEMI admissions (n=27,993) of patients aged ≥30 during 2001-2008 in 22 hospitals with a coronary angiography laboratory was studied. Data was collected from national hospital discharge registry (FHDR). Admissions with STEMI as primary (91%), secondary (7%) or tertiary (2%) discharge diagnosis were included. Hospital transfers during the same treatment period (14% of admissions) were combined. Majority (66%) of patients were men. The median age was 69 years.

Results: Total in-hospital mortality rate of STEMI was 11.9% (95%CI 11.5-12.2%). The unadjusted mortality rate was higher for men (HR 1:59; 95%CI 1.49-1.70, p < 0.0001). However, when adjusted for age and co-morbidities, there was no difference in mortality between genders (HR 1:00; 95%CI 0.93-1.07, p = 0.90). Mortality was highly dependent of age, with an estimated increase of 36% (95%CI 33.38%) per 5-year increase in age (p < 0.0001). STEMI was complicated by ventricular arrhythmia/resuscitation or pneumonia/pleuritis in men more commonly in men. In contrast, women had anterior infarction more commonly. Additional independent predictors of in-hospital mortality in multivariate regression analysis were ventricular arrhythmia/resuscitation (HR 2:05; 95% CI 1.73-2.43, p < 0.0001), pneumonia/pleuritis (HR 1:17; 95%CI 1.02-1.33, p = 0.05), peripheral artery disease (HR 2:30; 95%CI 1.81-2.93, p < 0.0001), malignancy (HR 1:80; 95%CI 1.42-2.28, p < 0.0001), neurological or neurovascular disease (HR 1:20; 95%CI 1:46-2.05, p < 0.0001) and diabetes (HR 1:17; 95%CI 1:03-1.33, p < 0.05). In-hospital mortality of STEMI was reduced during 2001-2008 by estimated 3.5% (95% CI 2.0 - 4.9%) per year (p < 0.0001).

Conclusion: In-hospital mortality of STEMI does not appear to be affected by gender itself, but increases significantly with age and co-morbidities.

P2644 | BEDSIDE

Prognosis of acute myocardial infarction associated to occlusion of the circumflex artery

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Background and aim: In the context of ST elevation myocardial infarction (STEMI) the traditional 12-lead electrocardiogram is sometimes not sufficient to detect the occlusion of the circumflex artery (CX). The European guidelines recommend utilization of 7, 16 and 9 leads in patients who present with chest pain and without significant electrocardiographic changes.

In daily clinical practice of emergency department those leads are rarely made. We intend to compare whether patients with acute myocardial infarction (AMI) secondary to occlusion of the CX are more often diagnosed with non-ST elevation myocardial infarction (NSTEMI) compared with patients with AMI due to occlusion of other epicardial arteries and assess whether this group of patients undergoing primary angioplasty, has a worse in-hospital prognosis.

Methods: We analysed 2306 patients included in a prospective national registry of Acute Coronary Syndromes with admission diagnosis of AMI between 01/10/2010 and 10/11/2013 and who had occlusion of one major epicardial coronary artery in the coronary angiography which was considered the culprit lesion. Patients were divided into 3 groups according to the occluded artery: Group 1 – left anterior descending artery (LAD); Group 2 – CX; Group 3 - right coronary artery (RCA). Each group was divided into 2 subgroups according to the classification of the AMI: Subgroup A: NSTEMI and B: STEMI.

Results: Of the 2306 patients, 1014 (44%) were included in group 1, 384 (16.7%) in group 2 and 908 (39.4%) in group 3. The % of patients with an epicardial artery occlusion (culprit lesion) and classified as NSTEMI in groups 1, 2 and 3 was 30.8, 37.7 and 31.5, respectively. In-hospital mortality in groups 1 and 3 was higher for subgroups B when compared with their homonyms of subgroup A (7 vs 0.7%, p = 0.004; 4.6 vs 0%, p = 0.009, respectively) while for group 2 there was a nonstatistically significant difference between the 2 subgroups (4.8 vs 1.7%, p = 0.101).

Among the subgroups B, there was a tendency for performing primary angioplasty later. The occlusion of the CX was associated with occlusions of LAD and RCA (door balloon time: 165±156 and 148±156, respectively, p = 0.08).

Conclusion: Patients with AMI due to occlusion of the CX are most often classified as NSTEMI, with consequent delay in revascularization. It should be reinforced the importance of the realization of V7, V8 and V9 leads in any patient with chest pain and no significant electrocardiographic changes.

P2645 | BENCH

Prognostic importance of tricuspid annular plane systolic excursion in acute myocardial infarction with ST segment elevation

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Tricuspid annular plane systolic excursion (TAPSE) is method to measure the distance of systolic excursion of the right ventricular (RV) annular segment along its longitudinal plane. TAPSE represents longitudinal function of the RV, in the same way as mitral annular plane systolic excursion by Doppler tissue imaging detects the movement of the left ventricle. TAPSE was applied for quantification of the myocardial contractility of RV and depends on ejection fraction of left ventricle (LVEF) as well.

The aim of this study is to evaluate the prognostic importance of TAPSE in acute phase of left ventricular inferior wall STE elevation myocardial infarction (STEVF).

Patients were 136 patients with left ventricular inferior wall STEMI who were admitted to hospital within 6 hours of the first symptoms of STEMI and treated by intravenous thrombolytic agents and/or coronary angioplasty. The echocardiographic examination was done within 48 hours of STEMI onset to measure LVEF and TAPSE. TAPSE was measured as the total distance displacement of the tricuspid annulus from end-diastole to end-systole.

The study subjects were divided into 2 groups, according to the TAPSE values. 58 patients fall into group A with TAPSE value ≤14 mm and 78 patients fall into group B with TAPSE value >14 mm. All subjects were taken into the 10 days hospital follow up.

There were no significant differences in basal characteristics of patients (age, male/female gender, % of hypertension and diabetes mellitus).

In-hospital mortality was significantly greater in group A (5/58 pts.-8.62%) than in group B (4/78 pts.-5.12%) (p = 0.05). Several ventricular arrhythmias and atrial fibrillation were observed in 19/58 patients of group A (32.7%) and in 11/78 patients of group B (14.1%) (p = 0.05).

The degree of sinoatrial and absinotricular II-III degree blockages were significantly higher in group A (10/58 pts.-17.24% vs. 6/78 pts.-7.69%) (p = 0.05).

There were no significant differences in LVEF values between patients groups. The incidence of right ventricular involvement in inferior wall STEMI is significantly higher in group A (3/58 pts.-53.44%) than in group B (4/147 pts.-17.94%) (p < 0.01).

Patients with inferior wall STEMI and right ventricular myocardial infarction (RVI) had significantly lower TAPSE value (16.7±1.9 mm) than patients without RVI (20.5±2.1 mm) (p = 0.01).

In acute phase of inferior wall STEMI TAPSE value ≤14mm is associated with higher in-hospital mortality and severe complications. TAPSE was significantly lower in patients with RVI than in patients without RVI and these patients have a worse prognosis.
following an index STEMI involving a previously non-culprit vessel is relatively low. Planned revascularisation of non-culprit vessels in a timely manner may explain this finding.

P2647 | BEDSIDE Survival in patients with ST-segment elevation myocardial infarction and significant versus non-significant coronary artery disease
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Purpose: There is limited knowledge on the prognosis of patients presenting with suspected ST-segment elevation myocardial infarction (STEMI) and non-significant coronary artery disease (CAD) where revascularization therapy is not indicated. We aimed to study survival in patients with suspected STEMI and significant versus non-significant CAD.

Methods: We included all patients receiving acute coronary angiography (CAG) with suspected STEMI at a high-volume PCI center during a 3.5 year period (2009-2013). Significant CAD was defined as coronary artery stenosis diameter ≥50% with indication for revascularization or, if not technically possible, medical treatment. Non-significant CAD was defined as either a normal CAG or CAD with coronary artery stenosis diameter <50% with no indication for revascularization. Patients were followed from the time of CAG to the event of death or end of study period. The Kaplan-Meier method was used to estimate survival probabilities.

Results: We included 3,407 patients with suspected STEMI, of which 418 patients (12%) had non-significant CAD. The median follow-up time was 460 days (interquartile range 186-733 days). Compared to patients with significant CAD, patients with non-significant CAD were younger and more frequently women with a lower body mass index and a lower prevalence of hypertension, smoking, and family history of ischemic heart disease. The risk of death within 30 days and 3 years was 3% (95% confidence interval [CI] 1-4%) and 13% (95% CI 8-17%) for patients with non-significant CAD compared to 7% (95% CI 6-8%) and 17% (95% CI 15-19%) for patients with significant CAD. Having non-significant CAD was associated with a lower risk of death (hazard ratio [HR] 0.69 [95% CI 0.49-0.96], p=0.028). However, after adjusting for age this was no longer statistically significant (HR 0.82 [95% CI 0.59-1.14], p=0.237). Additional adjustment for gender and multiple cardiovascular risk factors did not change the association further (HR 1.16 [95% CI 0.75-1.81], p=0.501).

Conclusion: In a large single center study of patients with suspected STEMI, we found no difference in short- or long-term survival between patients with significant versus non-significant CAD when the age difference between the two groups was taken into account. This finding suggest that acute chest discomfort in combination with ST-segment elevation but with absence of significant CAD is not trivial and may warrant further medical attention.

P2648 | BEDSIDE Comparison of the ability of CADILLAC and TIMI risk scores to predict short- and very long-term mortality in STEMI patients undergoing primary PCI

Purpose: Early risk stratification in STEMI patients is of prognostic and therapeutic importance. Our aim was to compare the ability of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) and the Thrombolysis In Myocardial Infarction (TIMI) risk scores to predict short- and very long-term mortality in patients undergoing primary PCI.

Methods: We examined 845 consecutive STEMI patients who underwent primary PCI in a high-volume catheterization laboratory in 2009. Separate logistic regression models were created for CADILLAC and TIMI risk scores. Predictive accuracy of both models was assessed by comparing ROC curves.

Results: Overall mortality at 30 days and four years was 5.8% and 20.1% respectively. CADILLAC risk score showed strong predictive accuracy for both 30-day and four-year mortality (C=0.87, 95%CI: 0.85-0.89 and C= 0.81, 95%CI: 0.78-0.84). Albeit less accurate, TIMI risk score was also predictive of 30-day (C=0.82, 95%CI: 0.79-0.84) and four-year mortality (C= 0.73, 95%CI: 0.70-0.77). Comparison of ROC curves showed more accurate predictivity of the CADILLAC risk score, as compared to the TIMI, for four-year mortality (p=0.0005), and a trend towards better predictivity for 30-day mortality (p=0.066). At 30 days the Hosmer-Lemeshow test revealed good model fit for the CADILLAC (p=0.51), but poor agreement of predicted and observed mortality for the TIMI risk score (p=0.063). At four years both CADILLAC and TIMI had good model fit (p=0.44 and p=0.16, respectively).

Conclusion: Both TIMI and CADILLAC risk scores appear to be accurate predictors of short- and very long-term mortality in STEMI patients undergoing primary PCI. CADILLAC risk score appears to have more discriminatory power than TIMI risk score, at both 30 days and four years.

P2650 | BEDSIDE Should we recommend the use of betablockers in patients with preserved left ventricular ejection fraction after an acute myocardial infarction treated with primary angioplasty?

Objective: The aim of this study was to analyze if betablockers after a ST-elevation myocardial infarction (STEMI) in patients with preserved left ventricular ejection fraction (LVEF) reduces mortality in the current era of primary angioplasty.

Methods: This was a retrospective analysis which included 820 consecutive STEMI patients discharged with preserved LVEF ≥50%. We assessed the incidence of death during follow-up (median 3.3 years, interquartile range 1.9 - 5.3 years) using multivariate Cox regression models, stratifying by GRACE risk groups and success of percutaneous coronary intervention (PCI).

Results: Betablockers were given in 78.5% of patients, in who the mortality rate was lower (5.6% vs 19.3) in comparison with no-betablocker group. After multivariate analyses, betablocker use was not a significant independent predictor of follow-up mortality (Hazard Ratio [HR] 0.658, 95% Confidence Interval [CI] 0.371 to 1.169). After stratifying by GRACE risk categories and by success of PCI, post-discharge betablocker therapy showed a protective effect only in high-risk patients (HR 0.262, CI 95%: 0.164 to 0.419) and in those with incomplete revascularization (HR 0.468, CI 95%: 0.227 to 0.980).

Conclusion: The only subgroups of post-STEMI patients with preserved LVEF underwent primary PCI that have long-term benefit in reducing mortality are those at high GRACE risk and those with incomplete revascularization.

P2651 | BEDSIDE LDL cholesterol levels in asymptomatic post-ACS patients remain above ESC targets despite statin treatment

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Background: Limited data are available on LDL cholesterol levels during one year follow-up in asymptomatic patients stabilised after acute coronary syndrome (ACS) admission treated with statins.

Purpose: Describe 1-year LDL patterns in asymptomatic post-ACS patients treated with statins.
Methods: BIOMACS is an observational study of ACS patients in 18 hospitals in our country. Treatment is left to the discretion of the physician. During 1 year follow-up, 20 repeat non-fasting blood samples are taken at preset time intervals. Serum and plasma are separated and stored on site at -80°C within 2h, until batch analysis in the central laboratory of the Erasmus MC. This abstract describes 100 patients treated with statins, who remained free of death, readmission for ACS, coronary revascularisation and anginal symptoms until 400 days. We determined LDL with the Roche Cobas c system in their repeated samples.

Results: Mean age was 65 (SD 5) years. 79% were men, 64% had STE-ACS. Patient profile was typical for an ACS population. In the 400-day period a total of 1691 blood samples were collected, with a median of 18 (IQR 15 to 19) per patient. Median LDL was 2.31 (IQR 1.93 to 2.74) mmol/l, LDL above 1.8 mmol/l was observed in 81% of samples; levels above 2.6 mmol/l were found in 33% of all patients (37% of patients). The within-patient variability was related to their mean LDL level (figure), but, within patients, LDL varied randomly between follow-up visits. Overall, the within-patient variability explained 30% of total variation and was thus smaller than the between-patient variability. (Data on total and HDL cholesterol are available).

Conclusions: Asymptomatic post-ACS patients treated with statins do not reach LDL targets recommended by the ESC guidelines.

P2652 | BEDSIDE
Long-term outcomes in patients switching from angiotensin-converting-enzyme inhibitors to angiotensin receptor blockers after incident ST elevation myocardial infarctions
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Purpose: Angiotensin-converting enzymes inhibitors (ACEI) are recommended for patients with ischemia heart disease to reduce the risk of death and nonfatal cardiovascular events. Angiotensin receptor blockers (ARB) are the alternatives for patients intolerant to ACEI. It is not known whether the ARB users switched from ACEI is as effective as non-switchers. We conducted a nationwide cohort study to evaluate the effectiveness of ARB on survivors of acute ST-elevation myocardial infarction (STEMI) in Taiwan.

Methods: A population-based inception STEMI cohort was constructed by using the Taiwan National Health Insurance claims data between year 2002 and 2010. Only survivors of the first STEMI with ACEI treatment during and after the index hospitalization were included. We excluded patients who had ever been treated with ACEI/ARB within one year preceding the STEMI, and was treated with ARB before ACEI prescription. Outcome was defined as death after index hospitalization. Cox proportional models adjusting for sex, age, years of hospitalization, comorbidities and medication was applied to estimate the effects of ARB on all-cause mortality. Inverse probability treatment weighting was then incorporated to deal with time-varying exposure.

Results: Total 17,498 patients were received ACEI therapy after index hospitalization, including 4,575 ARB switchers. Cumulative incidence of deaths was 2.75% in ARB switchers and 3.53% in non-switchers (P=0.012). After multivariate analyses, ARB did not significantly reduced the risk of mortality (adjusted HR, 0.86; 95% CI, 0.71 to 1.05; p=0.131) with inverse probability treatment weighting, including 4,575 ARB switchers. Cumulative incidence of deaths was rated to deal with time-varying exposure.

Conclusions: Asymptomatic post-ACS patients treated with statins do not reach LDL targets recommended by the ESC guidelines.

P2654 | BEDSIDE
Medical therapies in the emergency setting of patients not undergoing invasive workup
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Purpose: Patients with acute coronary syndrome (ACS) do not necessarily undergo coronary angiography and are managed acutely in a noninvasive manner. We investigate how soon evidence based secondary prevention therapies should be started after an ACS in this population.

Methods: The study populations consisted of 8214 ACS patients, of these 4156 patients (42.0% non-ST-elevation (STE) ACS and 58.0% STE-ACS patients) that did not received reperfusion treatment. Patients were admitted at 57 hospitals with a minimum of 10 patients reporting data to the International Survey of Acute Coronary Syndromes in Transitional Countries (ISACS-TC) registry (ClinicalTrials.gov. NCT01218776), from October 2010 to February 2014. We assessed the use of beta-blockers, statins and angiotensin-converting enzyme inhibitors in the emergency setting, (within 24 hrs since hospital admission) and their effects on in-hospital incidence of death.

Results: There were 2451 patients that received all 3 drugs in the emergency setting (group 3), 982 patients with 2 medications (group 2), 384 patients with 1 medication (group 1) and 252 patients that did not receive any drugs (group 0). The mortality rate was 4.8%, 11.1%, 29.2% and 65.7% in group 3, 2, 1 and 0, respectively. Benefits were observed both in non STE-ACS (incidence of mortality: 3.0%, 9.0%, 19.7% and 58.7%, in group 3, 2, 1 and 0, respectively) and in STE-ACS (incidence of mortality: 6.1%, 13.1%, 34.7% and 68.8% in group 3, 2, 1 and 0, respectively). The advantage of multiple combination of prevention therapies was confirmed by multivariable analysis. The absolute risk reduction was of greater magnitude and statistical significance (p<0.001) in those patients with non STE-ACS (adjusted OR: 0.11, 95%CI: 0.04-0.26) than in those with STE-ACS (adjusted OR: 0.07, 95%; 0.04-0.11).

Conclusions: Concomitant use of secondary prevention therapies in the emergency setting is associated with reduced of in-hospital mortality for those ACS patients not undergoing invasive workup.
Prognosis of new-onset atrial fibrillation in patients with acute coronary syndrome
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Background: Few studies have previously explored the potential prognostic role of different types of atrial fibrillation (AF) in patients with acute coronary syndrome (ACS). We conducted a retrospective cohort study to determine the prevalence and the prognostic implications of new-onset AF in patients with ACS admitted to a Coronary Care Unit (CCU).

Methods: We analyzed 5,640 patients with ACS admitted to a CCU (STEMI 2,690 and NSTEMI 3,130) and identified patients with preexisting, new-onset (AF at the moment of admission or developed during CCU stay) or no AF, to determine the incidence and prognosis at the CCU in the setting of ACS.

Results: A total of 299 patients were diagnosed with AF (5.1%). Preexisting AF accounted for 15% of all cases, whereas new-onset AF accounted 3.1% of the cases (AF at admission, 1% of AF, at the CCU, 2.1%). The prevalence of AF at the CCU in patients with STEMI was 2.6% and 1.7% in the NSTEMI group. All-cause mortality was significantly higher in the groups with AF at the CCU (15.1%) or preexisting AF (12.1%), in comparison to patients with AF at the moment of admission (3.1%) or no AF. The risk of death (OR 3.23, CI 95% 1.93-5.92, stroke (OR 6.18, CI 95% 1.83-20.87), cardiogenic shock (OR 3.28, CI 95% 1.63-6.62), inotropic requirements (OR 4.07, CI 95% 2.61-6.33) and vasopressors requirements (OR 4.89, CI 95% 3.7-7.2) was higher in patients with new-onset AF that developed during the CCU stay.

Conclusions: The presence of AF among patients with ACS has different prognostic implications. The new-onset AF developing during the CCU stay is probably a marker of severity and may be used as an independent predictor of all-cause mortality.
P2661 | SPOTLIGHT
Association of peripheral-blood transcriptome with prognostic markers of myocardial damage assessed by cardiovascular magnetic resonance after repertusfed ST-elevation myocardial infarction
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Purpose: Aim of the present study was to identify associations of global gene expression in peripheral blood mononuclear cells (PBMC) with established cardiovascular magnetic resonance (CMR) markers of myocardial damage and prognosis after ST-elevation myocardial infarction (STEMI).

Methods: We enrolled 106 patients with STEMI (70.0% men, age 60.8±11.9 years) after primary angioplasty within 12h after symptom-onset [median pain-to-balloon time 237 min (IQR 150–376)]. After reperfusion [median time interval 19.5 hrs (IQR 15–25)] whole blood was collected to perform high throughput transcriptome analysis in isolated PBMC using Illumina HumanHT-12 v4 Expression BeadChips. Subsequently, T2-weighted, SSFP-CINE, and contrast-enhanced CMR was performed within one week after infarction to assess the left ventricle ejection fraction (MR-EF), the myocardial salvage index (MSI), and to visualize late microvascular obstruction in relation to the infarct size [late MO/IS].

Results: After pre-processing accounting for relevant confounders, expression levels of 9949 genes were analysed. Among these, expression of one gene involved in the regulation of protein stability correlated strongest with MR-EF [p-value = 1.7x10-17; false discovery rate (FDR) = 0.21]. Another four genes were associated with late MO/IS at a FDR < 0.05 (corresponding to p < 9.4x10-10). No relevant links were found for MSI. Considering the top-associated transcripts at a less stringent cut-off p-value, KEGG pathway and gene ontology enrichment analysis was performed. MR-EF was found to associate with genes involved in posttranslational protein modification (24-fold enrichment, p = 3.0x10-9) and nucleoside metabolism (5-fold enrichment, p = 2.0x10-5).

Conclusion: We identified several candidate gene transcripts in association with CMR-predictors of prognosis after STEMI, providing potential targets for translational research strategies.

P2662 | BEDSIDE
Prognostic importance of cardiac troponin in the era of the universal definition: observations from an unselected hospital cohort
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Purpose: In 2007 the universal definition of myocardial infarction (MI) was introduced. We set out to study the prognostic importance of this re-definition in the setting of hospitalized pts having cardiac troponin measured for a suspected acute MI.

Methods: During a one-year period we prospectively studied unselected pts admitted to a university hospital. All pts having troponin I (cTnI) measured were included. The MI diagnosis was according to the universal definition, including typical rise/fall cTnI pattern, symptoms, ECG changes or imaging evidence of an acute MI. A cTnI value > 30 ng/L was considered the decision limit for the diagnosis of MI. Pts were followed for at least one year with all-cause mortality as the clinical endpoint. Multivariate Cox regression analysis was performed.

Results: From January 2010 to January 2011 totally 3762 qualified for inclusion. Of these 488 had MI, 1089 had cTnI > 30 ng/L but did not fulfill the MI diagnosis (TnI-), and 2185 had no cTnI elevation (TnI-). Pts were older (mean age 75±14 years) than MI (mean age 71±13 yrs) and TnI- pts (mean age 63±17 yrs) (< 0.0001). Pts also had significantly more co-morbidities: diabetes, renal failure, heart failure and COPD. During a median follow-up of 2.1 years 1085 pts died. Mortality differed between the groups: MI pts 31%, TnI+ pts 51%, and TnI- pts 18% (p < 0.0001; figure). In multivariate Cox regression analysis the hazard ratio for cTnI+ pts was 1.9 (95% CI 1.6-2.3) and for MI pts 1.5 (95% CI 1.3-1.9) when compared with cTnI- pts.

Conclusion: In the era of the universal definition more than two-thirds of pts with cTnI elevation do not have an acute MI. Indeed, the long-term mortality in these pts is significantly higher than in pts with a diagnosed acute MI.

P2663 | BEDSIDE
Cardiac troponin I for prediction of clinical outcomes and cardiac function through three months follow-up after primary percutaneous coronary intervention for ST-elevation myocardial infarction (STEMI)
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Purpose: Circulating levels of cardiac troponin I (cTnI) following ST-elevation myocardial infarction (STEMI) are associated with infarct size and chronic left ventricular dysfunction, but the relation to clinical endpoints and biochemical measures of global cardiac function remains less well-defined. The objective of this study was to investigate whether various cTnI variables were associated with clin-
chronic kidney disease (CKD). However, it is unclear whether the benefit of statin therapy is different between patients with and without CKD after ST-elevation myocardial infarction (STEMI) in the contemporary percutaneous coronary intervention (PCI) era.

Methods: From the database of the Osaka Acute Coronary Insufficiency Study, the present study enrolled 2,947 consecutive STEMI patients (median 65 y.o., 78.5% male, and 92.1% underwent PCI) whose serum creatinine was measured median 19 days after the onset. CKD was defined as having estimated glomerular filtration rate <60 ml/min/1.73m². The impact of statin therapy for 5-year mortality and re-myocardial infarction (ReMI) was assessed using multivariable Cox regression analysis in patients with and without CKD. Adjusted covariates included age, gender, classical coronary risk factors, enrollment year, infarct size, KILLIP, PCI, and medications at discharge.

Results: A long study population, 1,099 patients (37.3%) had CKD. There were 190 all-cause death and 128 ReMi events during 5-year follow-up. Statin therapy was associated with lower mortality in all study population (adjusted hazard ratio (HR) 0.65, 95% confidence interval 0.45-0.93, p=0.017) without significant difference between patients with or without CKD (p for interaction=0.373). In contrast, statin therapy was associated with lower ReMi events only in patients with CKD, but without CKD (p for interaction=0.005) (Figure).

Conclusions: Our results suggested that benefit of statin therapy for ReMi was different between patients with and without CKD after STEMI in the contemporary PCI era, while it was comparable for mortality. Further study is warranted to confirm our results.

P2665 | BEDSIDE

Estimation of renal function in patients with acute coronary syndrome: different equations, different risks?
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Purpose: Chronic kidney disease has an unquestionable negative impact on the prognosis of patients (P) with acute coronary syndromes (ACS). Traditionally, eGFR is estimated by MDRD equation (Eq). Three new equations recently emerged, based on serum creatinine (CKD-EPI Cr), serum cystatin-C (CKD-EPI Cc) or combination of both (CKD-EPI Cr/Cc). These equations have already been validated in renal dysfunction screening, however, studies in the area of ACS are scarce. The aim of this study was to compare the prognostic value of these Eq on prediction of long-term mortality (M) in P admitted for ACS, and to determine the best Eq and compare it with traditional MDRD as well.

Methods: Study of 801 P (67±13.3y, 68.5% male) admitted for ACS in a cardiac care unit along 3 years, in which the serum Cr and Cc were determined at admission. P were considered as belonging to a high risk group (HR) if GFR<60ml/min/1.73m² and low risk (LR) if GFR≥60ml/min/1.73m². Follow-up regarding M was performed.

Results: According to the different Eq, P were considered to be high risk in 29.8% by MDRD, 30.6% by CKD-EPI Cr, 28.3% by CPK-EPI Cr/Cc and 27.3% by CKD-EPI Cc. Mortality on follow-up (23.7±9.8 months) was 18.1%, and all Eq showed to be predictors of this endpoint (p<0.001). However, CKD-EPI Cc is the Eq that included a greater number of P with events in the HR group (39.7%), followed by the CKD-EPI Cr/Cc (37.0%), CKD-EPI Cr (32.7%) and MDRD (32.2%). Comparison of these 4 Eq through ROC curves confirmed that CKD-EPI Cc has the highest ability to predict M (AUC 0.726), being superior to all others Eq (p<0.001).

Conclusion: According to the different Eq, P were considered to be high risk in 29.8% by MDRD, 30.6% by CKD-EPI Cr, 28.3% by CPK-EPI Cr/Cc and 27.3% by CKD-EPI Cc. Mortality on follow-up (23.7±9.8 months) was 18.1%, and all Eq showed to be predictors of this endpoint (p<0.001). However, CKD-EPI Cc is the Eq that included a greater number of P with events in the HR group (39.7%), followed by the CKD-EPI Cr/Cc (37.0%), CKD-EPI Cr (32.7%) and MDRD (32.2%). Comparison of these 4 Eq through ROC curves confirmed that CKD-EPI Cc has the highest ability to predict M (AUC 0.726), being superior to all others Eq (p<0.001).

Conclusion: Our results suggested that benefit of statin therapy for ReMi was different between patients with and without CKD after STEMI in the contemporary PCI era, while it was comparable for mortality. Further study is warranted to confirm our results.

P2660 | BEDSIDE

Interaction of chronic kidney disease and statin benefit could be different between 5-year mortality and re-infarction in patients who survived ST-elevation myocardial infarction
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Purpose: Statin therapy can reduce cardiovascular risk even in patients with
P2667 | BEDSIDE
Post-Extrasystolic T-wave changes predict late mortality after myocardial infarction
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Background: Post-extrasystolic T-wave change (PEST) is a phenomenon described first by PD White in 1915. He observed that the T-wave of the first normal beat after a ventricular premature complex often is altered with magnification, decrease or a change in the direction of the T-wave vector. This observation was confirmed in many experimental studies. In a contemporarily-treated cohort of acute MI patients, we tested whether PEST provides prognostic information and how this information compares to that of established risk assessment.

Methods and results: 941 consecutive patients (mean age 61 years, 19% female) presenting with acute MI were enrolled between May 2000 and March 2005. All patients underwent 30-minute recordings of high resolution ECG (1.6 kHz sampling of orthogonal XYZ leads), 224 patients showed VPCs during the these 30-minutes. We quantified PEST by two variables (1) change in T-wave area and (2) change in the angle of the T-wave vector in each case compared to the average of three T-waves before and after the first postextrasystolic beat. PEST was defined as ratio TPEST:T>3 area >1 and ratio TPEST:T≤3 angle ≥5°. PEST was independent of standard risk predictors. PEST presumably indicates abnormal transmural gradient in repolarization time.

Conclusions: PEST is significantly associated with mortality in patients with acute myocardial infarction. PEST was independent of standard risk predictors. PEST presumably indicates abnormal transmural gradient in repolarization time.

P2668 | BEDSIDE
In-hospital and long-term mortality for patients 80 years or older with acute ST-segment elevation myocardial infarction. An eastern Norway cohort study 2005-2011

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Purpose: Patients ≥80 years with ST-elevation myocardial infarction (STEMI) are underrepresented in clinical trials, and little is known about long-term mortality of STEMI patients ≥80 years. The percentage undergoing coronary angiography and PCI if indicated, was lower in patients ≥80 years compared to younger patients. Although in-hospital mortality was relatively low in patients treated invasively, only 58% were alive after 2 years.

Methods: Single-centre observational cohort study. All consecutive STEMI-patients admitted to our hospital between 01.09.2005 and 31.12.2011 were included in a local registry. Predefined data including in-hospital mortality were registered. Vital status was obtained from the National Cause of Death Registry with censoring date 31.12.2011.

Results: A total of 4525 patients with a confirmed diagnosis of STEMI were registered; 600 patients (13%) were ≥80 years. The percentage undergoing coronary angiography and PCI if indicated, was lower in patients ≥80 years compared with younger patients (83% vs. 98%), but there was no difference in symptom-to-balloon times. In the total cohort, in-hospital mortality was 4% for patients <80 and 17% for patients ≥80 years. In the invasively treated patients (96% of all), in-hospital mortality was 3.4% in patients <80 years and 13% in patients ≥80 years. The median follow-up time was 2.5 years. Survival in invasively treated patients ≥80 years was 66% after 1 year and 58% after 2 years (Figure). Factors associated with long-term mortality were prehospital resuscitation, elevated serum creatinine and PCI.

Conclusions: Mortality after STEMI was high in patients ≥80 years compared to younger patients. Although in-hospital mortality was relatively low in patients treated invasively, only 58% were alive after 2 years.

P2669 | BEDSIDE
Worsening renal function is more strongly associated with long-term mortality than chronic kidney disease after ST-elevation myocardial infarction
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Purpose: Worsening renal function (WRF) is associated with worse outcomes in patients with left ventricular systolic dysfunction and heart failure. The purpose of the present study is to assess the prognostic impacts of WRF in patients with ST-elevation myocardial infarction (STEMI), drawing a comparison between WRF and chronic kidney disease (CKD).

Methods: From the database of the Osaka Acute Coronary Insufficiency Study, the present study enrolled a total of 2,782 consecutive STEMI patients (median 67 y.o., 77% male, and 94% underwent percutaneous coronary intervention) whose creatinine values both on admission and at discharge were available. We defined WRF as an increase in serum creatinine levels greater than 0.3 mg/dL from hospitalization to discharge for STEMI. CKD was defined as estimated glomerular filtration rate (e-GFR) less than 60 mL/min/1.73 m² at discharge. The impacts of WRF and CKD were assessed using multivariate Cox regression analysis for 5-year all-cause mortality after discharge.

Results: Among the study population, 10.9% had WRF and 51.6% had CKD at discharge. There were 142 all-cause deaths during a median of 716 (quartiles 214-1440) days follow-up. The adjusted hazard ratio and 95% confidence interval (CI) for 5-year mortality was 6.39 (3.15-12.94, p <0.001) for the presence of WRF, and 1.67 (1.11-2.52, p=0.0137) for CKD. Multivariate logistic regression analysis revealed that independent predictors of WRF were baseline creatinine on admission (adjusted odds ratio 1.89, 95% CI 1.14-3.06, p=0.011), body mass index (1.05, 1.01-1.09, p=0.012), and dyslipidemia (0.72, 0.53-0.96, p=0.039).

Conclusions: The impact of WRF for long-term mortality was greater than that of CKD after STEMI in the contemporary percutaneous coronary intervention era.

P2670 | BEDSIDE
In-hospital acquired anemia: prognostic predictor in acute coronary syndromes

Purpose: Admission anemia is a recognized predictor of poor prognosis in acute coronary syndromes (ACS). There is a growing interest in understanding the prognostic value of in-hospital acquired anemia, “nosocomial anemia” (NA). We sought to determine the prevalence, predictors and prognostic value of NA in ACS.

Methods: Retrospective study including 1345 P with ACS consecutively admitted to a coronary care unit over 3 years and during a minimal 6 months follow-up. NA was defined as an in-hospital hemoglobin (Hg) drop until WHO anemia diagnostic criteria, and was further classified as mild (Hg ≤11g/dL) or moderate/severe (Hg<11g/dL). P were excluded if they had admission anemia (n=321) or bleeding complications with hemodynamic instability/invasive treatment (n=17).

Results: During hospitalization, 329 P developed NA, these P were older (59.1±12 vs 66.1±13y; p<0.001) and more often had hypertension (65.5% vs 59.1%; p=0.04), chronic renal failure (3.0% vs 1.2%; p<0.001) and atrial fibrillation (7.6% vs 4.4%; p=0.04). At admission, they had lower mean levels of eGFR (<12 vs 15.0±1.2 g/dL; <0.001) and higher levels of creatinine (1.0±0.4 vs 0.9±0.3mg/dL; p=0.001), type B natriuretic peptide (3187±5097 vs 1489±2553pg/mL; p<0.001) and C-reactive protein levels (20.8±39.9 vs 10.5±21.9mg/L; p<0.001). The echocardiographic evaluation showed that they
had more often left ventricular systolic dysfunction (LVSD) (56.8% vs 47.1%; p<0.001) and mitral regurgitation grade ≥IIIV (14.9% vs 6.6%; p<0.001). During hospitalization, they had a higher incidence of respiratory infections (7.9% vs 1.8%; p<0.001) and heart failure (38.6% vs 18.4%; p<0.001). They were more often managed with more aggressive treatments, including the use of inotropic agents (p<0.001) and intra-aortic balloon (p=0.004). Femoral vascular access for cardiac catheterization was performed more often in P with NA (10.0% vs 5.2%; p=0.002). After multivariate analysis, admission Hg, respiratory infections and LVSD persisted as independent predictors of NA. In hospital (4.3% vs 0.9%; p=0.001) and 6 months (4.3% vs 1.1%; p=0.03) mortality was higher in P with NA. In-hospital major adverse cardiovascular events were also higher in this group (45.0% vs 15.9%; p<0.001), but this trend didn't persist in follow-up. Moderate/severe NA was an independent predictor of in-hospital (OR 2.5; CI95%: 1.0-6.3) and 6 months mortality (OR 2.1; CI95%: 1.1-4.0) versus the lowest (7.4%/year) CXCL16 quartile (HR 1.63 95% CI [1.22-2.18], p=0.004 in comparison to the lowest quartile). For OPG there was an increased risk of the primary outcome in the two higher quartiles (11.2 and 11.4%/year) (HR 1.64[1.21-2.12] and 1.68 [1.24-2.28], p<0.0002 in comparison to the lowest quartile 8.8%/year). No significant interaction between biomarkers and effect of randomized treatment on the primary outcome was observed.

Conclusions: In patients with ACS higher serum levels of CXCL16 and OPG are associated with clinical risk factors and adverse outcome but did not identify subgroups of patients with specific benefits from more intense antiplatelet therapy.

P2674 | BENCH
The classical CD14++ CD16- monocyte count is a risk factor for coronary artery disease
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Purposes: The white blood cell and neutrophil count has been considered as risk factors for coronary artery disease (CAD), while the data of monocytes’ role in CAD is rare. Monocyte can be classified as classical and non-classical monocyte by absence or presence of CD16 surface molecule and each monocyte subset has different functional characteristics in atherosclerosis. Therefore, we hypothesized that monocyte subset rather than total monocyte count might be associated with CAD.

Methods: We enrolled 208 consecutive patients (mean age; 63±11 years, M:F=121:87) with stable (SAP) or unstable (UAP) angina and control patients whose coronary angiogram showed no significant stenosis. We measured percent of each monocyte subset using flow cytometry. After gating mononuclear cells by forward and side scatter properties, monocytes were subdivided according to the surface expression pattern of CD14 and CD16.

Results: The median (interquartile range) of CXCL16 was 5.10 (4.4 – 6.0) and 4.55 (3.8 – 5.5) in SAP and UAP patients, respectively (p<0.001). Butyrylcholinesterase showed a protective effect on survival free of cardiac mortality in the entire study cohort with an adjusted HR per one standard deviation (1-SD) of 0.90 (95% CI 0.53-0.93, p=0.01). A significant interaction between butyrylcholinesterase and age groups was found (p=0.008). Analysis of the age strata showed the strongest protective effect in the age group 45-64 years with an adjusted HR per 1-SD of 0.28 (95% CI 0.12-0.64, p=0.03), and a decreasing association with mortality with increasing age (85-84 years: adjusted HR per 1-SD 0.66 [95% CI 0.40-1.06], p=0.087; >85 years: adjusted HR per 1-SD 0.84 [95% CI: 0.58-1.38], p=0.613).

Conclusion: Butyrylcholinesterase is a specific predictor for cardiac mortality in younger patients with ACS with an age between 45 and 64 years, while no significant association could be detected in all other age classes. The exact pathophysiological mechanisms and the age-dependent effect of butyrylcholinesterase on cardiac mortality need to be elucidated in future studies.

INFLAMMATION AND ACUTE CORONARY SYNDROMES

P2673 | BENCH
Chemokine (CXC motif) ligand 16 (CXCL16) and osteoprotegerin (OPG) as predictors of outcome in patients with acute coronary syndromes (ACS) a PLATO biomarker substudy
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Background: The number of acute coronary syndrome (ACS) in young people (<65 years) is continuously rising. While a large quantity of prognostic factors in ACS are already established less attention has been paid to their age-dependent prognostic value and their relevance in younger patients so far. The aim of our study was to assess the age-dependent prognostic impact of butyrylcholinesterase, which has been shown to be inversely associated with cardiac mortality.

Methods: We retrospectively included 624 patients with ACS into our cohort study. Patients were randomized and stratified into equal groups (n=208 per group) according to age <45-64 years, >65-84 years and "over 85 years". Cox regression hazard analysis was used to assess the influence of butyrylcholinesterase on survival. The multivariate model was adjusted for clinical covariates and OPG may play a modulatory role in platelet-mediated vascular inflammation and, at least partly, represent different inflammatory pathways. We evaluated factors associated with OPG and CXCL16 levels, their relation to 1-year outcome and interactions with platelet inhibition in patients with ACS.

Methods: CXCL16 and OPG levels were determined in serum collected at randomization to clopidogrel or clobazol in 4185 patients with ACS in the PLATO (PLATElet inhibition and patient Outcomes) trial. Baseline characteristics by Chi-square test (categorical variables) or Kruskal Wallis test (continuous variables), and occurrence of the primary outcome, a composite of cardiovascular death, non-fatal myocardial infarction, or stroke (n=362), by Cox proportional hazards models were compared between groups stratified by quartiles of the respective biomarker.

Results: The median (interquartile range) of CXCL16 was 5.10 (4.4 – 6.0) and of OPG 2.6 (2.0 – 3.8) in patients with higher CXCL16 and OPG serum levels were older and more frequently female and had a medical history including hypertension, diabetes mellitus, angina pectoris, heart failure, PCI, and chronic renal disease. In addition, patients with higher CXCL16 but lower OPG had a higher frequency of smoking, prior PCI, angina pectoris and ST-elevation MI. Higher CXCL16 levels in younger patients (<65 age group) according to age "45-64 years", "65-84 years" and "over 85 years".”

Conclusion: NA was a common complication in ACS. Moderate/severe NA was an independent predictor of in-hospital and 6 months mortality. Admission Hg, respiratory infections and LVSD were independent predictors of NA.
Inflammation and acute coronary syndromes

P2676 | BEDSIDE

LDL cholesterol and triglyceride levels are independent predictors of cardiovascular events in HIV-HCV co-infected patients: ANRS CO3-HIV-RUHR

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Purpose: HIV infection increases the risk of mortality with cirrhosis, liver failure and hepatocarcinoma in HIV co-infected patients. The risk and spectrum of cardiovascular diseases (CVD) in this population are not well assessed with contradictory previous results.

Methods: We used the French prospective multi-center HEPAVII-ANRS CO313 cohort, to prospectively collect all CVD events, atherosclerotic [coronary death, acute coronary syndrome, coronary revascularization, ischemic stroke, peripheral arterial disease], and cardiovascular events [cardiovascular death, myocardial infarction, or stroke] occurring during the entire follow up. Chi 2 test was used for qualitative variables and Wilcoxon test for quantitative variables to screen potential CVD predictors. A Cox model was performed to identify CVD predictors among adjusted selected parameters. P-value < 0.10 in univariate analysis.

Results: Among 1175 HIV-HCV co-infected patients (70% men, mean age: 45.0 years) included from January 2006 to January 2008 and followed till September 2013 (median follow-up: 57.6 months), we observed 42 CVD events overall and 21 cardiovascular events (5.6% of men and 10.5% of women). LDL cholesterol showed the highest levels of pro-inflammatory NCM (15.2±7% vs. 11.4±6% and 10.9±4%; p<0.01) when compared with patients in the middle (sdLDL-2 to 3mg/dL, T2) and lowest tertile (sdLDL-<2mg/dL, T1). Furthermore, LDL cholesterol was increased in women, independently of other CV risk factors and hsCRP. In contrast, when adjusting for CV risk factors and S100A/A9, hsCRP was associated with incidence of cardiovascular death in women and not men. Neither biomarker predicted the incidence of stroke.

Conclusion: Our results support the value of S100A/A9 as an important biomarker in the screening and follow-up of cardiovascular events. Further studies on potential mechanisms are needed.

P2676 | BEDSIDE

Association of small dense LDL serum levels and circulating monocyte subsets in patients with stable coronary artery disease

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Background: Atherosclerosis is considered to be an inflammatory disease in which monocytes and monocyte-derived macrophages play a key role. Circulating monocytes can be divided into three distinct subtypes, namely classical monocytes (CM; CD14++CD16-), intermediate monocytes (IM; CD14++CD16+) and non-classical monocytes (NOM; CD14+CD16+). Low density lipoprotein particles are heterogeneous in size and density, with small, dense LDL (sLDL) crucially implicated in atherogenesis. The aim of this study was to examine whether monocyte subtypes are associated with sLDL subfractions and circulating monocytes.

Methods: We included 90 patients with angiographically stable coronary artery disease and determined monocyte subtypes by flow cytometry. sLDL was measured by an electrophoresis method on polyacrylamide gel.

Results: In the high-density group of patients with sLDL levels >4.4mg/dL (n=35), we showed the highest levels of pro-inflammatory NOM (15.2±7% vs. 11.4±6% and 10.9±4%; p<0.01) when compared with patients in the middle (sdLDL-2 to 3mg/dL, T2) and lowest tertile (sdLDL-<2mg/dL, T1). Furthermore, LDL cholesterol was increased in women, independently of other CV risk factors and hsCRP. In contrast, when adjusting for CV risk factors and S100A/A9, hsCRP was associated with incidence of cardiovascular death in women and not men. Neither biomarker predicted the incidence of stroke.

Conclusion: Our results support the value of S100A/A9 as an important biomarker in the screening and follow-up of cardiovascular events. Further studies on potential mechanisms are needed.

P2679 | BEDSIDE

Role of cytokines as a risk factors of cardiovascular diseases in patients with rheumatoid arthritis

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Comorbid medical conditions are common in patients with rheumatoid arthritis (RA). First brought to light with observations of increased mortality in RA, studies noted the increased rates of cardiovascular events (Michaud K., F. Wolfe, 2007). A characteristic feature of rheumatoid arthritis (RA) is an imbalance between the overproduction of proinflammatory cytokines predominantly macrophage nature: tumor necrosis factor-α (TNF-α), interleukin-1, interleukin-6 (α) and the reduction of anti-inflammatory cytokines: interleukin-10 (IL-10) and IL-6. In recent years, IL-1, 6, and TNF-α has given increased importance in the formation of hypertension and atherosclerosis (Mazur V., 2005).

The aim of the study was to reveal the relationship between the level of IL-1 and TNF-α in serum and indicators of cardiovascular diseases in patients with RA.

Materials and methods: 565 RA patients (diagnosis according to the criteria of ACR/EULAR 2010) from the rheumatology in-patient clinic with the mean age
43.4±10.95.4%ACCP-positive patients; II. III activity on DASS28. 85.6% female and duration of the disease 3-15 years were reviewed. The level of cytokines (IL-1, TNF-α) were estimated with the use of ELISA. We assessed blood pressure (BP), level of LDL, triglycerides (TG) and hs-CRP.

**Results:** Analysis of the results revealed the statistically significant increase level of IL-1 and TNF-α in the serum of RA patients (p<0.01). We revealed statistically significant correlation between the level of cytokines (IL-1, TNF-α) and parameters of cardiovascular diseases: BP r=0.742 (p<0.01); LDL r=0.621 (p<0.01) and α=0.578 (p<0.05) accordingly; TG r=0.512 (p<0.01) and r=0.364 (p<0.05); hs-CRP r=0.821 (p<0.01) and r=0.964 accordingly.

**Conclusion:** Proinflammatory cytokines (IL-1, TNF-α) may be indirect risk factors of development and progression for hypertension and atherosclerosis in patients with rheumatoid arthritis, which should be considered when examining patients and the prescription of basis therapy.

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**P2680 | BEDSIDE**

**Ghrelin receptor deficiency aggravates instability of atherosclerotic plaque and vascular inflammation in low-density lipoprotein receptor-null mice**

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Ghrelin has been found to be associated with anti-inflammation, inhibition of atherosclerotic plaque formation and plaque stability in cardiovascular system. We investigated whether ghrelin affected the atherosclerotic plaque and immune inflammation of atherosclerosis. We crossed ghrelin receptor knock out mice (GHSR−/−) into a low-density lipoprotein receptor-null (LDLR−/−) mouse line. In this model, atherosclerotic lesions were promoted by feeding a high-fat, high-cholesterol Western-type diet for 18 weeks, following a standard protocol. The plaque burden (aortae) and the expression of ICAM-1 and VCAM-1, T cell, macrophage and smooth muscle cells of atherosclerotic plaque were observed. Though the serum lipid levels and atherosclerotic plaque area on aortic arches were not significantly different between GHSR−/−+LDLR−/− mice and GHSR−/−/LDLR−/−, the protein expression of ICAM-1 and VCAM-1 in atherosclerotic plaque was increased in GHSR−/−+LDLR−/− mice than that in GHSR−/−/LDLR−/− mice. T cell and macrophage were more, while the smooth muscle cells of atherosclerosis plaque were less in GHSR−/−+LDLR−/− mice than that in GHSR−/−/LDLR−/− mice. In conclusion, ghrelin receptor deficiency aggravates instability of atherosclerotic plaque and vascular inflammation but not atherosclerotic plaque area, which will provide novel avenues for the treatment of atherosclerosis patients.

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**P2681 | BEDSIDE**

**Monocyte subpopulation counts and function are associated with global longitudinal strain in patients with normal ejection fraction after ST elevation myocardial infarction**

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Purpose: The relationships of subclinical inflammation biomarkers, autonomic imbalance and anxiety and depressive syndromes in patients with myocardial infarction (MI).

Methodology: Patients with ST-segment elevation MI, mean age 61.4±1.6 years, were enrolled. At days 5-7 the heart rate variability was assessed, plasma inflammatory biomarker concentrations (high-sensitivity C-reactive protein – CRP, interleukins IL-1β, IL-6, IL-8, IL-10, interferon - INF-γ, tumor necrosis factor - TNFα) were measured by ELISA and psychometric testing used the Zung Self-Rating Depression scales, State-Trait Anxiety Inventory (Spilberger-Hanin) was done. The data were analyzed using the STATISTICA 6.0 software package (StatSoft).

Results: Patients with depression and increased levels of state and trait anxiety had significantly higher CRP and INF-γ plasma concentrations as compared to those without depression or anxiety symptoms. Depression was associated with significantly higher concentrations of inflammatory cytokines IL-1β (72.2±1.3 vs. 50.7±1.5, p=0.01) and INF-γ (94.4±2.8 vs. 71.8±2.3, p=0.001) as well as with the sympathetic nervous system activity, as assessed with the SDNN. In the group of patients with myocardial infarction, who had marked increase in the sympathetic nervous system activity (SDNN <70 ms), the levels of IL-1β, IL-6, TNF and INF-γ were significantly higher as compared to those in patients with the normal SDNN values. Indeed, IL-1β levels were 164.5 (152, 174) and 108 (96, 110), respectively, IL-6 levels: 4.48 (2.2, 6.3) and 3.44 (2.4, 4.9) IL-8: 81.3 (76; 92) and 41 (28;51); TNFα levels: 37.4 (28.6, 44.4) and 26.3 (19.4, 3.6); INF-γ: 94.9 (91; 101.2) and 21.6 (18.3, 23), p<0.01 in all cases. The resulting differences did not depend on the severity of myocardial infarction.

Conclusion: The presence of myocardial infarction in patients with sub-acute symptoms of depression and increased anxiety is associated with more severe inflammatory and sympathetic activity, which may explain a well-known adverse prognostic role of anxiety and depression syndrome in MI.

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**P2682 | BEDSIDE**

**Role of inflammatory and sympathetic activation in anxiety and depression interaction with myocardial infarction**

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**Purpose:** To examine the relationships of subclinical inflammation biomarkers, autonomic imbalance and anxiety and depressive syndromes in patients with myocardial infarction (MI).

Methodology: Patients with ST-segment elevation MI, mean age 61.4±1.6 years, were enrolled. At days 5-7 the heart rate variability was assessed, plasma inflammatory biomarker concentrations (high-sensitivity C-reactive protein – CRP, interleukins IL-1β, IL-6, IL-8, IL-10, interferon - INF-γ, tumor necrosis factor - TNFα) were measured by ELISA and psychometric testing used the Zung Self-Rating Depression scales, State-Trait Anxiety Inventory (Spilberger-Hanin) was done. The data were analyzed using the STATISTICA 6.0 software package (StatSoft).

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Conclusion: The presence of myocardial infarction in patients with sub-acute symptoms of depression and increased anxiety is associated with more severe inflammatory and sympathetic activity, which may explain a well-known adverse prognostic role of anxiety and depression syndrome in MI.

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**P2683 | BEDSIDE**

**Subclinical inflammation quantified by Interleukin-6 for detection of exercise-induced myocardial ischemia**

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Background: Existing data support the assumption that subclinical inflammation and IL-6 are involved in the development of atherosclerosis, the pathophysiological hallmark of coronary artery disease (CAD). Nonetheless, clinical data evaluating the value of IL-6 measurements to detect functionally significant CAD are sparse. The aim of this study was to investigate the value of an Interleukin-6 (IL-6) measurement to detect exercise-induced myocardial ischemia (MIS).

Methodology: We included 1539 patients referred to our university hospital for CAD evaluation with rest/stress myocardial perfusion single photon emission tomography (MPI-SPECT). All clinical information available to the treating cardiologist was used to quantify the clinical judgment regarding the presence of MIS using a visual analogue scale prior to bicycle exercise stress-testing. IL-6 measurements were obtained before stress-testing in a blinded manner. The presence of MIS was adjudicated based on MPI-SPECT combined with coronary angiography findings.

Results: MIS was detected in 647 (42%) participants. IL-6 levels were significantly higher in patients with MIS (1.6 ng/l [95%CI 1.0-2.7] versus 1.3 ng/l [95%CI 1.1-2.0], p=0.001) and remained an independent predictor of MIS in multivariable analysis (p<0.005). Receiver operating characteristics (ROC) analysis showed only poor diagnostic accuracy of IL-6 for detection of MIS as quantified as area under the curve (AUC) of 0.59 (p=0.001). Combining clinical judgment prior to exercise testing with IL-6 levels revealed no relevant increase in diagnostic accuracy 0.67 (combination) vs. 0.65 (clinical judgement alone) (p=0.005).

Conclusion: Although statistically significant associated with MIS, IL-6 measurements do not seem to provide clinically relevant additional information to clinical judgement of the treating cardiologist in the detection of MIS in patients with suspected CAD.
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The relationship between neutrophil/lymphocyte ratio and infarct-related artery patency before mechanical reperfusion in patients with STElevation myocardial infarction

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Objectives: Reduced baseline coronary flow in infarct-related artery (IRA) before a primary percutaneous coronary intervention (PCI) increases mortality in patients with STElevation myocardial infarction (STEMI). Increased neutrophil/lymphocyte (N/L) ratio has been linked to poor clinical outcomes in patients with STEMI. We investigated whether the N/L ratio, as measured at admission, was associated with IRA patency before mechanical reperfusion in patients with STEMI undergoing PCI.

Patients and methods: A total of 404 patients who had undergone PCI on a single culprit artery were enrolled in this study. According to thrombolysis in myocardial infarction (TIMI) flow grade in the IRA before PCI, the study population was divided into two groups as TIMI 0 or 1 group (occluded IRA) and TIMI 2 or 3 group (IRA patency).

Results: The N/L ratios were found to be significantly higher in the TIMI flow 0/1 group when compared with the TIMI flow 2/3 group (6.08±3.94 vs. 4.01±2.87, P=0.001). The absence of early IRA patency was associated with higher Syntax score, mean platelet volume, CK-MB, and troponin T levels (P<0.001, P=0.03, <0.001, and P=0.04, respectively), and lower left ventricular ejection fraction (P=0.02). Multivariate logistic regression analysis showed that the N/L ratio and Syntax score were independent predictors of IRA patency (odds ratio: 1.89, 95% confidence interval: 1.82–1.96; odds ratio = 2.90, 95% confidence interval: 1.75–3.86, respectively, P<0.001).

Conclusion: The N/L ratio has been found to be associated independently with early IRA patency before PCI in patients who have undergone PCI for STEMI. This simple and cheap parameter can provide useful information on the related risk evaluation in these patients.

STABLE ANGINA: PROGNOSIS AND OUTCOME

P2666 | BEDSIDE

Assessment of chest pain: Results from a rapid access chest pain clinic in England

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Background: Patients referred to our Rapid Access Chest Pain Clinic (RACPC) are seen within 2 weeks; however, the referrals must fulfill certain criteria: 1) no previous history of ischaemic heart disease 2) chest pain less than 6 weeks duration and 3) never been investigated in the past. Exclusion criteria includes severe acute coronary syndromes, uncontrolled hypertension, left bundle branch block and male, younger than 30, and females younger than 40. We report findings from referrals to our RACPC in the year 2013.

Methods: All patients referred to our RACPC were included in this study and their details and outcome of investigations were collected prospectively.

Results: 367 patients were seen in the clinic during 2013. 12 referrals (3.3%) were deemed inappropriate as they did not meet the NICE referral criteria. Of the remaining 355 (54.1% male, 45.9% female), only 2% were younger than 40 and less than 6% had a previous history of ischaemic heart disease. On admission, 61-69 (36%), 183 patients underwent exercise tolerance testing (ETT) to aid further investigation and management. 52% of the total number of patients were referred for an angiogram and 13% for functional testing (ETT) to aid further investigation and management. 52% of the total number of patients were referred for an angiogram and 13% for functional testing (ETT) to aid further investigation and management. 52% of the total number of patients were referred for an angiogram and 13% for functional testing (ETT) to aid further investigation and management. 52% of the total number of patients were referred for an angiogram and 13% for functional testing (ETT) to aid further investigation and management. 52% of the total number of patients were referred for an angiogram and 13% for functional testing (ETT) to aid further investigation and management.

Conclusion: Despite the lack of CT calcium scoring capabilities, RACPC remains an invaluable service to investigate and manage patients with a new presentation and long term prognosis after percutaneous coronary interventions in patients with chronic ischemic heart disease in several studies. Nevertheless, these studies lacked long term follow up. The aim of the this study was to investigate the effects of His-TnT levels after successful, elective percutaneous coronary intervention in the patients with stable angina pectoris for predicting major adverse cardiovascular events within one-year.

Methods: 100 patients (76 males and 24 females) presented stable angina pectoris where Department of Cardiology in our University Hospital who underwent successful, elective percutaneous coronary intervention were included the study. The patients who are elevated troponin I levels before procedure (>0.1 ng/ml) were excluded from the study. His-TnT levels were measured at before procedure, 6-12, 24, and 36 hours after procedure. For the positive value of His-TnT level was considered > 14 pg/ml. The patients followed-up for major adverse cardiovascular events (death, acute coronary syndrome and stroke) along one-year.

Results: In the study; His-TnT levels were reached the positive value in 36% of patients before procedure and 63% of patients after procedure. For the positive value of His-TnT level was considered > 14 pg/ml. The patients followed-up for major adverse cardiovascular events (death, acute coronary syndrome and stroke) along one-year.

Conclusions: In the study; His-TnT levels were reached the positive value in 36% of patients before procedure and 63% of patients after procedure.

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Geriatric nutritional risk index predicts cardiovascular and all-cause mortality in chronic haemodialysis patients after coronary revascularization

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Background: Although coronary revascularization, regardless of surgical or percutaneous procedures, has been commonly performed in chronic haemodialysis (HD) patients with coronary artery disease, poorer prognosis still remains major problem in such population. Recently, protein-energy wasting (PEW) or malnutrition have been considered to be more closely associated with chronic inflammation and advanced atherosclerosis. We investigated whether geriatric nutritional risk index (GNI), developing as a simplified marker of the PEW, predicts cardiovascular (CV) and all-cause mortality after coronary revascularization in HD patients.

Methods: A total of 785 HD patients undergoing coronary revascularization (622 with percutaneous coronary intervention and 163 with coronary artery bypass graft) were examined. The GNI was calculated from pre-procedural tests, as follows: GNI = (14.89 × albumin) + [41.7 × body weight / body BMI]. In addition, patients were divided into quartiles according to GNI levels: GNI < Q1 (<88.6), Q2: 88.7–94.1, Q3: 94.2–99.3 and Q4: >99.4. They were followed up for up to 10 years.

Results: During follow-up period (median: 43 months), there were 250 cases of CV death, and 238 cases of all-cause death. After adjustment for other confounders, GNI [hazard ratio (HR) 2.55, 95% confidence interval (CI) 1.43-4.55, p=0.0016 for Q1 vs. Q4], age (HR 1.02, 95%CI 1.01-1.04, p=0.012), multi-vessel disease (HR 1.62, 95%CI 1.17-2.23, p=0.0032), ejection fraction (HR 0.98, 95%CI 0.97-0.99, p=0.0081) and C-reactive protein (HR 1.08, 95%CI 1.04-1.13, p=0.0001) were identified as independent predictors for CV mortality. GNI also independently predicted all-cause mortality (HR 2.30, 95%CI 1.42-3.72, p=0.0008 for Q1 vs. Q4).

Conclusion: Declined GNI which reflect PEW state was closely associated with both CV- and all-cause mortality after coronary revascularization in chronic HD patients.
patients with acute myocardial infarction, whereas the analogous data in patients with stable coronary artery disease (CAD) are scarce. The aim of this study was to assess the prevalence of AF in outpatients with CAD, and to determine clinical and laboratory correlates associated with the higher prevalence of this comorbid arrhythmia. Further, we compared the indications for antiarrhythmic therapy using the older CHADS2 and the modern CHA2DS2-VASc scale.

Methods: We investigated a representative sample of 2578 Polish patients with stable CAD participating in the multicenter RECENT study (age: 65±10 years; men: 55%; Canadian Cardiovascular Society [CCS] class III/IV: 38/48/14%). These patients were consulted by the primary care physicians and the specialists on an outpatient basis and the detailed medical history was obtained using a dedicated questionnaire.

Results: AF was present in 19% of patients with stable CAD. In simple comparisons patients with AF were older, had more comorbidities, higher resting heart rate, lower total cholesterol, higher creatinine, and declared the greater severity of angina (as assessed using CCS scale) and the longer history of CAD (all P < 0.05). In a multivariable logistic regression model, advanced age (prevalence of AF according to age > 65 [median] vs. ≤ 65 years: 24 vs. 15%, P = 0.001) and concomitant heart failure (HF) (with vs. without HF: 31 vs. 13%, P < 0.001) were independently associated with the higher prevalence of AF (all P < 0.05). In patients aged > 65 years, with CAD history of > 5 years, and with coexistent HF, the prevalence of AF was 40%. In patients with CAD and AF, according to CHA2DS2-VASc scale 73% of subjects required antithrombotic therapy (score ≥ 2) and according to CHA2DS2-VASc scale = 94% (score ≥ 2). 47% of patients with a CHADS2 score of 0 and 85% with a CHA2DS2 score of 1 had a CHA2DS2-VASc score ≥ 2. In summary, 21% of patients with CAD and AF did not have clear indications for antithrombotic therapy according to CHA2DS2 scale (score: 0)-1, while they required oral anticoagulation according to CHA2DS2-VASc scale (score ≥ 2).

Conclusions: AF affects every fifth ambulatory patient with CAD and in patients with a longer history of CAD and HF the prevalence is doubled. According to CHA2DS2-VASc scale almost all patients with CAD and AF require antithrombotic management, which makes the additional anticoagulation therapy challenging.

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Purpose: To assess whether a good control of cardiovascular risk factors (CVRF) or medical treatment will improve the quality of life on patients with stable angina. The AVANCE study. A national survey

Methods: Two thousand and twenty-four patients with SCAD were consecutively recruited in an observational, multicentric, transversal registry. Good control of CVRF was defined as: blood pressure < 140/90 mmHg; glycemia control, < 111 mg/dL for non-diabetic and < 126 mg/dL in diabetic patients; LDL cholesterol < 100 mg/dL; heart rate < 70 beats per minute. Seagull angina questionnaire (SAQ) questionnaire was filled by the patients.

Results: No CVRF or HR good control was present in only 25 patients. The number of well controlled CVRF was associated with younger age, male gender, heart failure, and had no association with stroke, optimal medical treatment (OMT, 52% of patients). Beta blockers (78% of patients), calcium channel blockers (40%), and statin (93%) were associated with better CVRF control, but not with antiplatelet therapy (96%), ACEI (41%) or ARB (32%). Bivariate analysis of all the items of the SAQ questionnaire were associated with the number of well controlled CVRF (QOL improved as more CVRF were controlled). On multivariant analysis, the number of well controlled CVRF had an independent association with satisfaction with treatment, stability of angina SAQ domains, but not on perception of disease, frequency of angina and physical limitation SAQ domains. OMT had no independent association with QOL as assessed with the SAQ.

P2691 | BEDSIDE
5-year-mortality and quality of life in the elderly with stable angina and documented coronary artery disease (CAD): Results of the STAR-Registry

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Background: First angiographic diagnosis of CAD is made at different ages dependent on onset of angina symptoms. Little is known about the 5-year-mortality and quality of life in the elderly compared to younger patients with newly diagnosed CAD.

Methods: Between Sep 2001 and March 2003, a total of 2,002 consecutive patients with angina pectoris and first angiographic diagnosis of CAD were enrolled in the STAR-Registry (50 centers). We compared outcome and quality of life in the elderly (>75 years) and in younger (<75 years) patients at 5 years follow-up.

Results: Elderly patients more often were female, had more concomitant diseases as well as 3-vessels CAD. There were no differences in the use of PCI during the 5 years follow-up. The elderly showed a significantly higher 5-year-mortality. In the group of survivors more than half of the elderly complained of impaired quality of life (EuroQol DS-5 Score).

P2692 | BEDSIDE
Fifteen years survival of patients with nonsignificant atherosclerotic changes of coronary arteries

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Hemodynamically nonsignificant atherosclerotic plaques are often found in patients undergoing coronary angiography. The aim of our study was to compare the survival rates in 3 groups of patients. The have found statistically significantly higher fifteen years survival for individuals with smooth coronary arteries (67%), compared with patients with significant coronary artery stenoses (61%) (Pcorr < 0.0001) and also with coronary artery irregularities (62%) (Pcorr < 0.01). In contrast, there was no statistical difference in survival between patients with significant atherosclerotic coronary artery disease and the group with nonsignificant changes. The differences were statistically significant even after including the effects of age and gender (smooth coronary arteries vs significant stenoses: p = 0.05, HR 2.25; smooth coronary artery vs insignificant atherosclerotic changes: p = 0.05, HR 2.57).

The results of our study indicate that long-term prognosis of patients with insignificant atherosclerotic changes is significantly worse than in individuals with smooth coronary arteries and roughly corresponds to patients with significant coronary artery disease. This finding supports the need for aggressive anti-atherosclerotic drug therapy in such individuals.

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Heart rate and quality of life in stable angina patients. AVANCE study. A national survey

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Purpose: To assess whether heart rate (HR) was associated with quality of life (QOL) in a national-wide survey of patients with stable coronary artery disease (SCAD).

Methods: Two thousand and thirty-nine patients with SCAD were consecutively recruited after obtaining the institutional, multiscientific, transversal registry. There were 85 patients where HR was not available. Therefore 1954 patients were studied. Good heart rate control was considered when HR was <70 bpm. Seattle angina questionnaire (SAQ) was filled by the patients.

Results: See Table. Patients with HR >70 bpm were more frequently women, had a higher rate of atrial fibrillation (AF), DM, hypertension, were more symptomatic (both angina episodes and number on GTN per week), and had a higher prevalence of comorbidities (i.e. stroke, COPD). There were also some baseline differences in medical treatment. HR >70 bpm was achieved in a 63% of patients. After adjustment with covariates significant at bivariate analysis, HR >70 bpm was independently associated with worse QOL (all items of SAQ but physical limitation).

Conclusions: HR >70 bpm was achieved in a 63% despite of extensive beta blocker use. HR >70 bpm is independently associated with QOL in patients with SCAD.

Gender-related differences in coronary atherosclerosis severity in patients with premature coronary disease

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Background: Coronary artery disease (CAD) remains the leading cause of death in Western and developing countries. Despite the advances in interventional and pharmacological treatment, in the group of young women with CAD mortality is even increasing. Reasons for this discrepancy remains unclear.

The aim of this study was to assess disease severity in women with premature CAD in comparison with men with premature CAD.

Materials and methods: The study prospectively included women and men with premature onset of CAD ≤55 and ≥45 yrs of age respectively, CAD was defined as presence of stenosis ≥50% in a major epicardial coronary artery on coronary angiography. The disease severity was assessed by the modified Duke Coronary Artery Disease Index which classifies ≥50% stenosis as clinically significant and evaluates the number of vessels involved and the location of stenosis. An obstructive coronary artery stenosis was defined as ≥75% stenosis in a major epicardial coronary artery and/or ≥50% stenosis in the left main (LM).

Results: The study included 283 women (men age 46.7±5.4yrs) and 240 men (mean age 39.6±4.4yrs). The mean value of modified Duke Coronary Artery Disease Index for entire group was 48.4±1.7; median 48. The mean value of the Index was higher in women as compared with men (49.9±1.7 vs 46.6±1.7; p=0.0035). There was no gender-related difference in number of patients who had at least one obstructive (>75%) stenosis in coronary arteries (91.2% of women vs 94.2 of men; p=0.24).

However, in women the obstructive stenosis was more frequently located in the proximal left anterior descending coronary artery (LAD) and/or LM than in men (53.7% vs 44.6%; p=0.044).

Female gender was a significant predictor of the higher (≥median) modified Duke Coronary Artery Disease Index, and of obstructive stenosis in proximal LAD and/or LM after adjustment for age, sex, hyperlipidemia, hypertension, diabetes and smoking (OR 2.14; p=0.002 and OR 2.2; p=0.0006 respectively).

Conclusions: Women with premature CAD as compared with men have more severe coronary disease burden. In patients with premature CAD women present with greater frequency of high-risk anatomy as compared with men, including significant proximal LAD and LM involvement.

Long-term clinical outcomes in patients with coronary artery disease and moderate angina pectoris treated with enhanced external counterpulsation therapy

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Background: Enhanced External Counterpulsation (EECP) therapy is a non-invasive circulatory assist device used commonly in the treatment of refractory angina. There are limited data on the long term outcomes of EECP therapy in patients with Class II angina. This study compares the EECP therapy, and 2-year survival rates of free of major adverse cardiovascular events (MACE: CABG, PCI, MI, death) for patients with moderate angina (Class II) and severe angina (Class III/IV) treated with EECP.

Methods: The International EECP Patient Registry enrolled patients from 90 centers. Patients were divided into two groups. Moderate Angina Group (MAG: Class II: N=257) and Severe Angina Group (SAG: Class III/IV; N=2848). Comparisons between groups were analyzed using chi-square and t-tests. Follow-up events were analyzed using survival methods.

Results: Age average age was 67 years in MAG and 66 in SAG. The previous invasive revascularization rate was lower in MAG (p<0.001); 81% in MAG and 90% in SAG had prior PCI or CABG. MAG had less hypertension, multivessel disease, congestive heart failure, prior MI and had lower rates of nitroglycerin usage and lower angina frequency (p<0.001). In both groups, patients were on optimal medical therapy as tolerated. After a mean treatment course of 34 hours, both groups showed a significant reduction in the severity of angina (78% vs 61%) Discontinuation of nitroglycerin usage was similar in both groups (>50%). MACE during the treatment period was low in both groups (<2%). Compliance with the treatment course was better in MAG (p<0.01).

At 2 year follow up 80% of MAG and 78% of SAG had maintained the improvement in angina class; 44% in MAG and 30% in SAG had no angina; discontinuation of nitro usage was maintained in both groups. Survival rate was 95% in MAG and 90% in SAG (p<0.001). MACE free survival rate was 82% in MAG vs 72% in SAG (p<0.001).

Conclusion: Patients presenting for EECP treatment with class II angina had different baseline profiles compared with Class III and IV angina. However, both cohorts achieved substantial reduction in angina with high event free survival rates at 2 years. For patients with stable Class II angina pectoris who were not candidates for further revascularization the best treatment options have not been fully defined. EECP appears to offer a safe and effective treatment option.

N-3 to N-6 polyunsaturated fatty acid ratio is associated with atheroma progression in patients achieving very low levels of low-density lipoprotein cholesterol

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Background: Enhanced reduction in low-density lipoprotein cholesterol (LDL-C) with statins produces regression or stabilization of coronary artery plaques. However, after achieving very low levels of LDL-C, atheroma regression is not always observed in all patients. The purpose of the present study was to evaluate the determinants of atheroma progression despite achieving very low levels of LDL-C.

Methods: The effects of 8-month statin therapy on coronary atherosclerosis were evaluated using virtual histology intravascular ultrasound in the TRUTH study. Of these, 33 patients who achieved an on-treatment LDL-C level of <70 mg/dl were divided into 2 groups according to increase (progressors) or decrease (regressors) in plaque volume.

Results: At the 8-month follow-up, serum LDL-C and apolipoprotein B levels were significantly lower in progressors than in regressors; however, significant increases in high-density lipoprotein cholesterol and apolipoprotein AI and decreases in high-sensitivity C-reactive protein and oxidized LDL were observed in both groups. The changes in the N-3 to N-6 polyunsaturated fatty acid ratios significantly differed between the 2 groups. Multivariate regression analysis showed that a decrease in the EPA : DHA:AA ratio was a significant predictor associated with atheroma progression (p<0.012, p=0.004)
Conclusions: N-3 to N-6 polyunsaturated fatty acid ratios affected coronary artery plaque progression and regression in patients who achieved very low levels of LDL-C during statin therapy.

CORONARY ARTERY DISEASE AND COMORBIDITIES

P2698 | BEDSIDE

Prevalence of cerebrovascular events, associated clinical profile and treatment of patients with stable coronary artery disease: the results of the multicentre RECENT study

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Introduction: Atherosclerosis is a chronic systemic disease, which often takes the multifocal form, occupying more than one distinct vascular areas. The magnitude of concomitant symptomatic coronary artery disease (CAD) and cerebrovascular disease (i.e. transient ischaemic attack (TIA) and/or stroke) remains unclear.

Methods: We analyzed data on 2,593 patients with stable CAD participating in the recently registered, constituting a representative group of the Polish outpatient CAD population.

Results: The prevalence of previous TIA and/or stroke among patients with stable CAD was 2.0% and 4.6%, respectively. Patients with atrial fibrillation (AF) accounted for 19% of this group. TIA and/or stroke occurred in 8% vs 17% of patients without vs with AF (p <0.0001).

Patients without AF with previous TIA and/or stroke were older, more often suffered from heart failure (HF), arterial hypertension, dyslipidemia in comparison to those with TIA and/or stroke (all p<0.05). Patients with AF and a history of TIA and/or stroke were older, more often had angina in CCS class II/III, HF and peripheral artery disease (PAD) as compared to those without TIA and/or stroke (all p<0.05).

We identified the following independent risk factors of higher prevalence of previous TIA and/or stroke in patients with stable CAD in a sinus rhythm: age of 65 years and more (11% vs. 6%), family history of CAD (12% vs. 7%), angina in CCS class II/III, hypertension (9% vs. 5%), dyslipidemia (10% vs. 6%) and PAD (17% vs. 7%) (all p<0.05). In patients with stable CAD and AF, the following risk factors were independently associated with the higher prevalence of previous TIA and/or stroke: angina in CCS class II/III (29% vs. 27%) and PAD (35% vs. 15%) (all p<0.05).

Patients in a sinus rhythm with a history of TIA and/or stroke were more likely to receive angiotensin converting enzyme inhibitors, angiotensin receptor blockers, loop diuretics and short-acting nitrates as compared to patients without neurologic complications (all p<0.05).

In the group of patients with AF, the history of TIA and/or stroke did not influence the applied treatment.

Conclusions: In a stable CAD population, almost every tenth patient in a sinus rhythm has suffered from cerebrovascular events, such as TIA and/or stroke, and among those with AF the risk has been almost doubled.

P2700 | BEDSIDE

Impact of coronary artery fixed lesion on 3-years clinical outcomes in vasospastic angina patients with myocardial bridge

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Background: It is not known whether the presence of angiographic fixed coronary lesion (FCL) can negatively impact on long-term major clinical outcomes in vasospastic angina patients (pts) with myocardial bridge (MB).

Methods: A total 5,882 pts (patients) underwent coronary angiography (CA) in our institute between Nov 2004 to Oct 2010. Among them, total 563 pts who had MB and documented significant coronary artery spasm (CAS) by Ach provocation test were enrolled. Study populations were categorized into two groups; the fixed coronary lesion (FCL) group (n=216) and the non-FCL group (n=347). Cumulative major clinical outcomes were compared between the two groups up to 3 years.

Results: Baseline characteristics were similar between the two groups except the incidence of elderly, hypertension, diabetes, and dyslipidemia were higher in the FCL group. In univariate analysis, only the composite end-point consisted of cardiac death, De Novo percutaneous coronary intervention (PCI), myocardial infarction (MI), and cerebrovascular accident (CVA) was higher in FCL group (Table). However, in multivariate regression analysis, the incidences of cardiac death, PCI, MI, CVA, recurrent chest pain, and other composite end-points were similar between the two groups up to 3 years.

Results:

P2699 | BEDSIDE

Coronary disease complications depend on pulse pressure dipping in old hypertensives

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Purpose: Pulse pressure, particularly estimated according to Ambulatory Blood Pressure Monitoring has recently played an increasing role in the cardiovascular risk assessment. The goal of our study was to evaluate the impact of diurnal pulse pressure profile on cardiovascular events in different age-groups of hypertensive patients with significant atherosclerosis established in coronary angiography. The present study is a part of PROGNOSIS study.

Methods: We enrolled 891 patients with coronary artery disease confirmed in angiography. 63.7±9.4 years of age. Clinic blood pressure measurement was performed and 24-hour ambulatory BP monitoring was obtained with BP readin 20 times in 26 observation intervals (06:52 AM – 06:00 PM) and at 30-minute intervals (06:00 PM – 06:00 AM). Pulse pressure was calculated as difference between systolic and diastolic blood pressure values. Pulse pressure dipping was calculated as percentage of decrease in nighttime pulse pressure in relation to daytime pulse pressure values. The studied subjects were divided into three age groups: <65 years of age, 65-74 years of age and >75 years of age. During a follow-up period of 6.7 years in total, cardiovascular events were assessed.

Results: In the group >75 years of age in comparison to group <65 years of age was observed higher values of 24 hour pulse pressure (60.7±12.3 mmHg vs. 49.4±9.9 mmHg, p<0.01), daytime (60.4±12.9 mmHg vs. 49.5±9.9 mmHg, p<0.01) and nighttime (61.3±12.4 mmHg vs. 49.2±10.6 mmHg, p<0.01). Moreover, nighttime pulse pressure/ daytime pulse pressure dipping ratio was significantly higher in patients >75 years of age in comparison to <65 years of age (1.1±0.1 mmHg vs. 49.2±10.6 mmHg, p<0.01). In the group >75 years of age in comparison to group <65 years of age higher total mortality (20% vs. 11%, p<0.05) and prevalence of major advanced cardiovascular event (42% vs. 30%, p<0.05) were observed. Only in the group >75 years of age pulse pressure dipping was associated with a hazard ratio of major advanced cardiovascular events of 1.1 (95%CI 0.96-0.99, p<0.03), and revascularization (percutaneous coronary angioplasty or coronary by-pass grafting) with a hazard ratio of 0.98 (95% CI 0.97-0.99, p<0.04).

Conclusions: Pulse pressure dipping is a good indicator related to major advance cardiovascular events and coronary revascularization in older hypertensive patients with coronary artery disease.

P2701 | BEDSIDE

Spontaneous coronary artery dissection single centre experience with systematic angiographic followup

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Introduction: Spontaneous coronary artery dissection (SCAD) is a rare cause of acute coronary syndrome. Evidence is based on single case reports, whereas only few larger case series have been published. In particular, there are no studies with systematic angiographic follow-up. We describe clinical characteristics, treatment, and angiographic follow-up of a contemporary SCAD population

Method: Over a 15 years period we systematically collected patients presenting with SCAD at our institution. A follow-up angiography was offered to all patients.

Results: There were 56 patients with SCAD (mean age 51±11 years, 93% females, three patients with peripartum SCAD). All patients had acute coronary syndrome. The following vessels were affected: left main (n=1), left anterior descending artery (n=25), left circumflex artery (n=28), right coronary artery (n=2). In 16 patients patient underwent coronary bypass grafting, five patients underwent percutaneous coronary intervention (PCI), and 51 patients were treated medically. One patient with peripartum left main SCAD died from cardiogenic and hemorrhagic shock during emergency PCI. All other patients were discharged in a stable coronary condition.

Conclusions: In our study, the presence of angiographic fixed coronary lesion in vasospastic angina pts with MB was not a predictor of adverse long-term clinical outcomes.
P2702 | SPOTLIGHT

Anemia prognosis significance on admission in patients undergoing percutaneous coronary intervention; up to 4 years of follow up

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Purpose: Anemia is common before percutaneous coronary intervention (PCI). Numerous studies have shown the prognostic value of anemia in patients with acute coronary syndrome (ACS). Few studies have investigated the long-term impact of pre-admission anemia of an admission in patients undergoing PCI and constitutes the aim of this study.

Methods: We performed a single-center observational study with prospective follow-up of 759 consecutive patients undergoing PCI between 2007 and 2011. Anemia was defined according to the OMS criteria (hemoglobin <13 g/dl in men and <12 g/dl in women). We evaluated the relationship between anemia with cardiovascular events and long-term mortality (mean follow-up 26.5±14.4 months).

Results: Anemia on admission was observed in 226 (29.8%) patients. Patients with anemia on admission were older (72.10±61.14 years, p<0.001), female (23.5% vs 15.2%, p=0.006), and diabetic (47.3 vs 31.5%, p<0.001) hyper-tense (76.1 vs 63.4%, p=0.001). Most often patients were previously treated with anti-coagulants (14.2 vs 7.3%, p=0.003) anti-platelets (58.4 vs 44.1%, p<0.001) had increased prevalence of acute myocardial infarction on admission (59.7% vs 42.9%, p<0.008), lower creatinine clearance (66.5±29.6 vs 78.9±23 ml/min/1.73m2, p<0.001) and higher levels of C reactive protein (35.5±54.5 vs 13.2±25.6 mg /l, p<0.001). While hospitalized had a higher incidence of contrast-induced acute kidney injury (15% vs 6%, p<0.001), bleeding complications (19.5 vs 8.6%, p<0.001), need for transfusion (6.6 vs 6%, p<0.001) and mortality (5.3 vs 1.5%, p=0.003). During long-term follow-up patients with anemia on admission had a higher incidence of readmissions (59.7% vs 47.7%, p<0.002), acute myocardial infarction with ST segment elevation (4.5 vs 1.7%, p=0.027), stroke (5.8 vs 2.1%, p=0.008) cardiac mortality (8.2% vs. 8% p=0.001) as well as all cause mortal-ity (20.4 vs 4.9%, p<0.001). Lastly, anemia on admission was associated to lower survival at follow up (45.3±1.5 vs 52.1±0.5 months, log-rank p<0.001). Cox proportional hazards analysis showed that the anemia was an independent predictor of all cause mortality (adjusted hazard ratio = 2.1, 95% confidence interval 1.1 to 4.1, p=0.028).

Conclusion: Patients with anemia on admission are numerous and have both poorer in hospital and long term prognosis as well as increased long-term mor-tality.

P2703 | BEDSIDE

Low-density lipoprotein cholesterol level on admission was predictor of in-hospital mortality in patients with acute coronary syndrome

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Methods: The primary aim of this study was to evaluate the long-term impact of car-diac troponin elevation on clinical outcome after major noncardiac surgery. Individuals with intermediate to high cardiac risk for major noncardiac surgery suffer from perioperative myocardial ischemic injury.

Results: Patients (n=750) aged ≥50 years who underwent major noncardiac surgery were eligible for the study. Postoperative cardiac troponin-I data were collected retrospectively. The primary outcome measure was all-cause mortality.

Conclusions: Besides well-known determinants, low HDL cholesterol level on admission was an independent predictor of in-hospital mortality in ACS patients.

P2704 | BEDSIDE

Troponin-I level after major noncardiac surgery and its association with long-term mortality: A retrospective cohort study with seven year period

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Purpose: The purpose of this study was to evaluate the long-term impact of cardiac troponin elevation on clinical outcome after major noncardiac surgery. Individuals with intermediate to high cardiac risk for major noncardiac surgery suffer from perioperative myocardial ischemic injury.

Methods: Patients (n=750) aged ≥50 years who underwent major noncardiac surgery were eligible for the study. Postoperative cardiac troponin-I data were collected retrospectively. The primary outcome measure was all-cause mortality.

Results: Up was 1727 days in all patients. Among 750 patients, 92 (12.2%) showed elevated postoperative troponin-I above 0.10 ng/mL. Operative mortal-ity was 4.1% (31 subjects), and patients with perioperative troponin-I elevation showed higher mortality rates (16.3% vs 3.1%, p<0.001). Odd’s ratio (OR) with 95% confidence interval [CI]: 7.26 – 14.0, p<0.001. In multivariate regression, postoperative troponin-I concentration above 0.10 ng/mL was associated with all-cause mortality (OR = 1.70, 95% CI 1.05 - 2.74, p<0.030). It should be noted that there was a significant difference between patients with elevated and non-elevated troponin-I in the rate of mortality until 6 months. However, these differences disappeared af-ter 6 months. In addition, age over 70 years, male sex, presence of chronic kidney disease, lower hemoglobin level, and heart rate more than 80 beats per minute were independent predictors of long-term mortality in major noncardiac surgery.

Conclusion: I level confers increase in mortality during the 7 year follow-up pe-riod after major noncardiac surgery. This difference of mortality was mainly de-rived from the result within the first six months.

P2705 | BEDSIDE

Vein grafts and progression of atherosclerotic disease after coronary artery bypass surgery

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Background: We sought to characterise patterns of native coronary artery dis-ease progression after primary CABG and to examine the effects of conduit type on disease behaviour.

Methods: 405 patients enrolled into a randomized study of coronary bypass con-duits underwent surveillance angiography as determined by trial protocol irre-spective of symptoms. Mean duration of follow up was 6.2±3.1 years. Each major native coronary vessel was interrogated and assigned a grade; Grade 0 is a non-flow-limiting lesion of 0-39%, grade 1 is a moderate lesion of 40-69%, grade 2 is a flow-limiting lesion of 70-80%, grade 3 is a severe lesion (81-99%) and grade 4 represents total occlusion (100%). Native vessel disease progression (NVPD) is defined as an increase of two or more grades of stenosis or progression to occlu-sion between the pre and post-operative angiograms. The presence of disease progression was correlated with vessel location and conduit type.

Results: NVPD occurred in 19.5% of all coronary vessels analysed and was similar across territories at 18.9%, 21.4% and 18.8% for the anterior, lateral and inferior territories respectively. Native arteries which were diseased at the time of surgery were more likely to progress than their un-diseased counterparts (27.9% vs. 12.4%, p<0.001). The presence of a saphenous vein graft was associated with significantly increased risk of progression, both when compared to analo-gous vessels receiving arterial conduits and to diseased vessels which were left ungrafted. Freedom from NVPD at 1, 5 and 10 years is estimated from 98.8%, 98.4% and 94.7% for the SVG with 98.2%, 97.8% and 93.7% for the RA (p<0.001) and with 98.2%, 88.6% and 58.7% for ungrafted vessels (p<0.018).

Discussion: Vein grafts are associated with increased risk of NVPD in addition to their poorer long term patencies compared with arterial grafts, making them an inferior conduit choice for revascularization.
Factors associated with CPAP acceptance in the patients with sleep apnea and cardiovas cilar disease

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Background: Although excessive daytime sleepiness (EDS) is one of the main symptoms of any cardia cal function, we examined the acceptance rates of CPAP in CVD patients with an AH1 greater than 20 and the factors associated with CPAP acceptance.

Methods: Data were collected from consecutive adult patients referred to our department of cardio-vascular medicine, university school of medicine unit from May 2010 to October 2012. We prospectively screened 309 patients with CVD for SAS using full polysomnography, and offered CPAP to 168 patients (54.4%) who meet the clinical criteria for CPAP therapy (AH1>20) regardless of their clinical symptoms and complaints. To determine the differences between acceptors and refusers, demographic variables, subjective sleepiness (Epworth Sleepiness Scale), polysomnographic variables, the types of sleep apnea, depressive symp toms and complaints. To determine the differences between acceptors and refusers, demographic variables, subjective sleepiness (Epworth Sleepiness Scale), polysomnographic variables, the types of sleep apnea, depressive symp toms and complaints.

Results: Most of subjects (91.1%) did not complain of EDS. Of the 168 patients, 70 patients (41.7%) were prescribed CPAP at baseline, 67 did not even try the CPAP titration, and the rest of 31 patients refused to use CPAP after one night of CPAP titration. CPAP acceptance was associated with higher EDS, lower QOL, higher subjective sleep disturbance (PSQI: CS) and higher obstructive sleep apnea index, but not age, AHI, PHQ-9, sleep architecture and any cardiac function.

Conclusion: CPAP acceptance is low in Japanese patients with CVD. The absence of subjective sleepiness in CVD patients may reduce the acceptance rate of CPAP.

Lipid profile after acute coronary syndrome in HIV-infected individuals. Results from the PACS-HIV case-control study


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Purpose: To compare the lipid parameters evolution and goals achievement between HIV-infected (HIV+) and uninfected individuals (HIV-) under statin therapy after acute coronary syndrome (ACS).

Methods: Fasting lipid parameters (Total Cholesterol, LDLc, HDLc, Non-HDLc, triglycerides, Total Chol/HDLc ratio) were collected during the prespecified 3-year follow up of the PACS-HIV study (Prognosis of Acute Coronary Syndrome In HIV-infected patients). The lipid goals were assessed using the updated NCEP-ATPIII guidelines. A mixed model for repeated measures was used to compare the evolution of lipid values over the entire follow-up between the two groups. Logistic regression was used to compare the probability of achieving the goal of lipid control.

Results: 95 HIV+ and 187 HIV- enrolled prospectively in the PACS-HIV study (mean age of the cohort 49 years, 94%, men) received statin therapy at month 1. At baseline, lipid parameters were similar in both groups except for a higher level of triglycerides in HIV+ (238.9±179.7 mg/dL vs 166.9±125.1 mg/dL, p=0.001). Six months after ACS a significant decrease of LDL-C was observed in the HIV- group (p=0.0001), while in the HIV+ group the decrease was not significantly different (p=0.06) (Figure 1). Concomitantly, the NCEP ATPIII goals for all athero genic lipid lipoproteins were less frequently achieved in the HIV+ group as compared to the HIV- group during the first 18 months. At 18 months, NECP ATPII LLD goal was reached by 43% of HIV+ and 72% HIV- patients, p=0.002 while at 36 months no significant difference was observed.

Conclusions: Early LDL decrease and LDL goal attainment are less frequently achieved in HIV+ as compared to HIV- during the first 18 months after ACS. This early higher residual cardiovascular risk warrants particular attention.

Low LDL cholesterol in acute myocardial infarction patients: friend or foe?


Introduction: High LDL cholesterol is both an etiologic and a prognostic factor in acute myocardial infarction (AMI). There is scarce literature concerning patients with ACS and low levels of LDL cholesterol (and not on statin therapy).

Objective: The aim of this study was to describe the rare population of patients with AMI and LDL below 100 mg/dL and to compare several clinical and analytical variables between this population and those with LDL levels ≥100 mg/dL or on statin therapy.

Methods: Retrospective observational study that included all AMI patients admitted to a single Coronary Care Unit at a tertiary hospital between January 2004 and August 2013. Patients were divided into two groups according to LDL cholesterol levels and compared to AMI patients with LDL ≥100 mg/dL and no previous statin therapy; group 2) patients with LDL<100 mg/dL or previous statin therapy.

Results: Retrospective analysis of 1169 AMI patients with clinical data concerning LDL cholesterol levels and previous statin therapy. 123 patients had LDL below 100 mg and were not on statins (group 1) and the remaining 1046 patients either had LDL levels equal or above 100 mg/dL or were on statin therapy (group 2). Group 1 patients were older (73±11 vs. 69±11, p<0.001) and had a higher BMI (27.0±4.4 vs. 28.1±4.3, p<0.012). Regarding past medical history, patients with lower LDL had a higher prevalence of Type 1 Diabetes Mellitus (11.6 vs. 4.0; p<0.001). Prevalence of other cardiovascular risk factors like hypertension, smoking, family history of coronary artery disease and type 2 Diabetes mellitus.
were not statistically different between groups. Patients with lower LDL had higher scores on GRACE score (156±40 vs. 142±35; p<0.001) and higher admission troponin (21.1±4.12 vs. 16.8±0.87; p=0.002) but coronary anatomy was not different between groups. Group 1 patients had higher creatinine levels (1.40±0.10 vs. 1.23±0.07; p=0.008) and lower estimated glomerular filtration rate (56.9±34.0 vs. 68±36.8; p<0.001) in hospital mortality rates were similar in both groups (6.5% vs. 4.4%; p=0.292).

Conclusion: This exploratory study found some intriguing associations in the rare population of patients with low LDL levels and acute coronary syndrome. In fact, as this population had a higher prevalence of type one diabetes mellitus and lower glomerular filtration rate, it is possible that the beneficial role of a low LDL level was superimposed by a higher prevalence of the former cardiovascular risk factors or blunted by the pleiotropic effects in the statin-treated cohort.

ACUTE CORONARY SYNDROMES – INTERESTING TOPICS

P2711 | BENCH
Age and gender differences in occurrence of ST-elevation myocardial infarction: a population based cohort study
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Purpose: Efficient and cost-effective coverage of 24/7 primary PCI service for ST-elevation myocardial infarction (STEMI) is problematic to establish and should be based on the STEMI risk of serviced population. We studied age- and gender specific risks of STEMI at the population level.

Methods: Age and gender differences in STEMI occurrence were studied using a nationwide, population based (n=26 736 956 person-years) registry of hospital admissions in patients aged >30 during 2001-2008. We included admissions with STEMI as primary (91%), secondary (7%) or tertiary (2%) discharge diagnosis. Hospitals with coronary angioplasty treat emergency patients (n=22) were included in study. Hospital transfers (14% of admissions) during the same treatment period were combined as one admission. Incidence was calculated using age and gender matched population data.

Results: The study period included 27 993 STEMI admissions of which 66.0% (95%CI 65.6-66.9%) occurred to men and 34.0% (95%CI 33.4-33.7%) to women. RR 2.37 (95%CI 2.05-2.74, p<0.001) during the study period. Female patients were significantly older than men (74.3±11.7 vs. 64.7±12.4 years, p<0.001). Age-standardized incidence of STEMI admission was 91.8 (95%CI 90.6-92.9) /100 000 person-years overall, 140.1 (95%CI 138.0-142.1) /100,000 in men and 52.1 (95% CI 50.9-53.3) /100,000 in women. Men had a 3.03 (95%CI 2.86-3.21; p<0.0001) fold age-adjusted relative risk of STEMI compared to women with highest risk difference in population under 55 years of age (RR 9.54; 95% CI 9.36-9.68, p<0.0001). Incidence increased with age up to 90 years-old, with estimated gender-adjusted increase rate of 4% (95%CI 40%-42%; p<0.0001) per 5-year increase in age. STEMI incidence had a slowly declining trend (−2.2%; 95%CI −3.4 to −1.0% per year, p<0.001) during the study period.

Conclusion: Men have a tripled overall risk for STEMI compared to women with highest relative risk in younger adults. Incidence of STEMI admissions increases with age by estimated rate of 41% per 5-years of age.

P2712 | BEDSIDE
Gender differences in the cardiovascular risk profile of patients admitted with ST-elevation myocardial infarction – results from the Bremen STEMI registry
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Introduction: While the importance of cardiovascular risk factors in the pathogenesis of coronary artery disease is well established there is few data on their association with gender in patients with acute myocardial infarctions. Aim of this study was to analyze gender differences of the cardiovascular risk profile in patients presenting with acute ST-elevation myocardial infarctions (STEMI).

Methods and results: Between 2006 and 2013 a total of n=5620 patients with STEMI were admitted to the Bremen heart center and then documented in the Bremen STEMI registry (n=5663; p=0.001). 4056 (72%) of patients were male and 1564 (28%) were of female gender. Since at time of STEMI women were on average older than men (69.3±13 yrs. vs 61.5±13 yrs., p<0.001) all data had to be adjusted for age. Patients were assigned to two groups: those with a first coronary event (first event, n=4505 (80%)) and those with previously known coronary artery disease (known CAD, n=1115 (20%) ). In patients with a first event women were more likely to show hypercholesterolemia (total cholesterol>240 mg/dl) and to be obese (BMI>30 kg/m2) than male patients while the prevalence of diabetes mellitus was lower in women. The proportion of active smokers showed no gender bias (Table). In patients with known CAD however the proportion of active smokers was lower in women than in men while the prevalence of hypercholesterolemia as well as obesity remained higher in women. However women were less often on medication with HMG-CoA reductase inhibitors (“statins”) prior to STEMI than men (18% vs. 23%, OR 0.74; 95% CI 0.67-0.81, p<0.001).

P2713 | BEDSIDE
Acute coronary syndromes in women of reproductive age
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Objectives: Data about younger women with Acute Coronary Syndromes (ACS) is very limited. The aim of this study was to compare women with ACS in the reproductive age compared with older women using a 20-year national registry.

Methods: Retrospective analysis of all women hospitalized with ACS in our country from 1991 through 2010 was made. Patients were divided into two groups according to age: age and clinical characteristics and outcomes were compared.

Results: During the 20-years period; 2472 women were hospitalized with ACS; 359 patients aged 15-49 years and 2113 patients aged 50 years and above. There was a significantly lower prevalence of diabetes mellitus, hypertension, chronic renal impairment and underlying ischemic heart disease in younger women compared to older women. Heart failure and atrial fibrillation were significantly more common complications in elderly women [table]. The inhospital mortality rate was significantly lower in women in the reproductive age compared to older women (7% vs. 11.2%; p<0.02).

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Women 15-49 yrs</th>
<th>Women 50 &amp; above</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in mean (years±SD)</td>
<td>43±6.5</td>
<td>65±10</td>
<td>0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m2) (mean ±SD)</td>
<td>31±7.7</td>
<td>30±7.1</td>
<td>0.09</td>
</tr>
<tr>
<td>Current smoker</td>
<td>21.5 (8.6)</td>
<td>68 (32.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>179 (49.9)</td>
<td>1503 (71.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>184 (51.3)</td>
<td>1441 (68.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Chronic renal impairment</td>
<td>12 (3.3)</td>
<td>152 (7.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>95 (26.5)</td>
<td>576 (27.3)</td>
<td>0.75</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>43 (12)</td>
<td>440 (20.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3 (0.8)</td>
<td>94 (4.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>Heart failure</td>
<td>26 (7.2)</td>
<td>323 (15.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>1 (0.3)</td>
<td>18 (0.9)</td>
<td>0.25</td>
</tr>
<tr>
<td>Total hospital stay (days, mean ±SD)</td>
<td>4.7±3.1</td>
<td>6±6.5</td>
<td>0.001</td>
</tr>
<tr>
<td>In-hospital Mortality</td>
<td>25 (7)</td>
<td>236 (11.2)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Data are expressed in numbers (%) of patients unless otherwise indicated.

Conclusions: Although the reproductive age have more favorable cardiovascular risk profiles, the observed mortality remains high. The current study underscores the need to study women in this age group in other ethnicities.

P2714 | BEDSIDE
Association of pre-infarction angina and total ischemic time with long-term survival in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention
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Purpose: The cardioprotective effects of pre-infarction angina in ST-segment Elevation Myocardial Infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PCI) are still controversial. This study aimed to investigate the influence of pre-infarction angina on clinical outcomes and assess the association of pre-infarction angina and total ischemic time with long-term survival in STEMI patients undergoing primary PCI.

Methods: The CREDO-Kyoto AMI Registry is a multicenter registry enrolling consecutive 5429 patients with acute myocardial infarction undergoing primary PCI from January 2005 to December 2007. Pre-infarction angina was defined as angina within 48 hours of hospital arrival for the index STEMI. The current study consisted of 3476 patients who underwent primary PCI within 24 hours of...
symptom onset and in whom the data on pre-infarction angina was available. The median follow-up period was 1845 days.

Results: Pre-infarction angina was present in 675 patients (19%). The infarct size estimated by peak creatinine phosphokinase was significantly smaller in patients with pre-infarction angina than in patients without pre-infarction angina (median: 2144 IU/L versus 2462 IU/L, p < 0.001). The cumulative 5-year incidence of death was significantly lower in patients with pre-infarction angina compared with patients without pre-infarction angina (12.4% versus 20.7%, p < 0.001). After adjustment for confounders, pre-infarction angina was independently associated with mortality (adjusted hazard ratio 0.69, 95% confidence interval 0.54-0.86, p < 0.001). According to total ischemic time (<3 hours: short, 3-6 hours: mid, or 6-24 hours: long), the cumulative incidence of death in patients with pre-infarction angina was consistently lower than that in patients without pre-infarction angina. Furthermore, the cumulative incidence of death in patients with pre-infarction angina in both mid and long total ischemic time was almost equal to that in patients without pre-infarction angina in short total ischemic time.

Conclusions: Pre-infarction angina was independently associated with lower 5-year mortality in STEMI patients undergoing primary PCI. The presence of pre-infarction angina as well as total ischemic time might be important as the determinants of long-term survival in STEMI patients.

P2715 | BEDSIDE
Identification of acute, spontaneous myocardial infarction in patients with atrial fibrillation and chest pain by use of a contemporary sensitive troponin I assay
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Introduction and aim: Introduction of more sensitive troponin assays has facilitated diagnosis of acute myocardial infarction due to improved sensitivity with corresponding loss of specificity. Atrial fibrillation is associated with elevated troponin levels independent of coronary status. The aim of the present study was to evaluate the diagnostic performance of troponin I in patients with suspected acute coronary syndrome and prevalent atrial fibrillation.

Material and methods: Contemporary sensitive troponin I (99th percentile cut-off 0.032 ng/mL) was assayed in a validation cohort of 90 patients with suspected acute coronary syndrome and prevalent atrial fibrillation. Additionally, changes in troponin I concentration within 3 h after admission were used as a diagnostic criterion.

Results: In the derivation cohort an unweighted optimized diagnostic threshold of 0.019 ng/mL was established. Application of the unweighted and the specificity-optimized cut-offs (0.019 ng/mL) and for a rule-in strategy with high specificity (0.09 ng/mL) were off 0.032 ng/mL and for a rule-out strategy with high sensitivity (0.019 ng/mL) was assayed in a validation cohort of 90 patients with suspected acute coronary syndrome (99th percentile cut-off). In patients with troponin levels above the specificity-optimized threshold upon admission, the diagnostic accuracy as quantified by the area under the ROC curve was 0.98 (95% CI 0.93-1.00) for hs-cTnT, 0.78 (0.65-0.87) for hs-cTnI, as well as 0.83 (0.75-0.89) for the combination of BNP and hs-cTnT and 0.84 (0.76-0.90) for the combination of BNP and hs-cTnI.

Conclusion: The dual-biomarker approach provides incremental value to clinical decision making in the diagnosis of suspected exercise-induced myocardial ischemia.

P2717 | BEDSIDE
Novel dual-biomarker strategy and clinical judgment in the detection of exercise-induced myocardial ischemia

Background: Assessment of coronary artery disease (CAD) currently is a resource-intensive process. The aim of this study was to investigate whether a novel dual-biomarker strategy quantifying two complementary pathophysiological signals (subclinical cardiomyocyte injury and hemodynamic cardiac stress) by measuring B-type natriuretic peptide (BNP) and either high-sensitivity cardiac troponin (hs-cTnT) or hs-cTnI can be used to diagnose exercise-induced myocardial ischemia in patients with known CAD.

Methods: We included 234 patients without previously known CAD referred for rest/stress myocardial perfusion single photon emission tomography (SPECT). BNP, hs-cTnT and hs-cTnI were obtained immediately before exercise testing in a blinded manner, followed by exercise stress testing. All clinical information available to the treating cardiologist was used to quantify the clinical judgment regarding the presence of myocardial ischemia using a visual analogue scale (VAS) twice: once prior and once after exercise stress testing. The VAS was then compared to the AUC obtained by logistic regression to combine the values of both biomarkers. The presence of myocardial ischemia was adjudicated based on perfusion SPECT combined with coronary angiography findings.

Results: Myocardial ischemia was detected in 49 (21%) participants. Median levels of biomarkers were significantly higher in patients with myocardial ischemia: BNP 50 [IQR 31-106] vs 112 [63-147] pg/mL, hs-cTnT 4 [2-10] vs 7 [4-19] ng/mL and hs-cTnI 2.3 [1.5-4] vs 3.4 [2.8-9.3] ng/mL. Diagnostic accuracy as quantified by the area under the ROC curve was 0.69 (95% CI 0.63-0.75) for BNP, 0.664 (0.599-0.724) for hs-cTnT, 0.719 (0.657-0.775) for hs-cTnI, as well as 0.726 (0.665-0.783) for the combination of BNP and hs-cTnT and 0.743 (0.683-0.798) for the combination of BNP and hs-cTnI.

Conclusion: The dual-biomarker approach provides incremental value to clinical decision making in the diagnosis of suspected exercise-induced myocardial ischemia.

P2718 | BEDSIDE
Role of CHADS2 and CHA2DS2-VASc scores for predicting subsequent myocardial infarction, stroke and death in patients with acute coronary syndrome
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Aims: Patients with acute coronary syndrome (ACS) present with a wide spectrum of risks for subsequent cardiovascular ischemic events and death. No simple and common scoring system is used to identify patients at high risk of adverse outcome. The aim of the study was to investigate whether the CHADS2 and CHA2DS2-VASc scores were useful risk assessment tools for adverse events in patients with ACS.

Methods and results: This observational, prospective study was conducted at 39 hospitals in Taiwan. Patients with ACS who were admitted were enrolled if they signed informed consent. We calculated the CHADS2 and CHA2DS2-VASc scores based on the data collected. The primary end point was the occurrence of adverse event, including subsequent myocardial infarction (MI), stroke and death at one year post-discharge. Of the 3163 patients enrolled, 1,665 (52.3%) patients were with acute coronary syndrome without ST-segment elevation (unstable angina) and attendant SH. Control group includes 22 patients (F:M: 16/6, mean age 61.1±3.4 years) with acute coronary syndrome without ST-segment elevation (unstable angina) with normal thyroid function. All patients determined concentration of cardiac troponin T (cTnT), underwent electrocardiography, echocardiography, Holter monitoring, and most of them (61%) – coronary angiography.

Results: The patients with unstable angina and attendant SH showed significantly higher median concentrations of cTnT than patients with normal thyroid function (0.6±0.2 versus 0.4±0.1 ng/mL, p<0.01). Also significant but inverse and weaker correlation was obtained between cTnT level and left ventricular ejection fraction (r= 0.061, p<0.01). Painless myocardial ischemia in patients with unstable angina and attendant SH was observed 2.2 times more frequent than in control (54.5% versus 25.2%; p<0.01).

Conclusion: We observed close relationship between subclinical hypothyroidism and painless myocardial ischemia.

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diagnosed with ST elevation MI. The rates of MI, stroke or death continuously increased with increasing CHADS2 and CHA2DS2-VASC scores. The CHADS2 and CHA2DS2-VASC scores were significant predictors of adverse events in separate multivariate regression analysis. After adjustment, the hazard ratio of the CHADS2 or CHA2DS2-VASC score for predicting future MI, stroke or death was 1.44 (95% CI 1.30-1.58, p < 0.001) and 1.36 (95% CI 1.26-1.46, p < 0.001), respectively. The Kaplan-Meier analysis based on the CHADS2 and CHA2DS2-VASC scores >2 obtained a higher rate of adverse events than when based on scores <2 (both log rank, p < 0.001). In addition, CHA2DS2-VASC score improved diagnostic performance in predicting subsequent adverse events when compared with the CHADS2 score with the area under the receiver operating characteristic curve increased from 0.66 to 0.70 (p < 0.001). The CHA2DS2-VASC scores could be used to further stratify the patients with CHADS2 scores of 0 or 1 into 2 subgroups with different rates of adverse events at a cutoff value of 2 (4.1% vs. 10.7%, p < 0.001).

Conclusions: CHADS2 and CHA2DS2-VASC scores are useful predictors for subsequent adverse events in ACS patients and may be helpful for identifying high-risk patients.

P2719 | BEDSIDE
De novo atrial fibrillation during acute coronary syndromes: which is the best therapeutic strategy?

Introduction: De novo atrial fibrillation (nAF) is frequent during acute coronary syndromes (ACS), being associated with morbidity and mortality. The current literature concerning the best therapeutic approach to nAF in this context is meager. Objectives: Describe and compare nAF therapeutic strategies during ACS, namely the rate (RaM) versus rhythm management (Rym) and the antithrombotic treatment.

Methods and results: We performed a prospective study including 902 consecutive patients (374 MI, 528 unstable angina) admitted in a Coronary Unit for the period of 2 years, with a 6 month follow-up. The atrial fibrillation (AF) rhythm was identified in 13.8% P, from whom 73.3% presented nAF and 26.8% previously known AF. From the 84 P with nAF, 27.4% were submitted to RaM and 72.5% to Rym. Between those whose RyM strategy was applied, 30.0% went home with antiarrhythmic therapy to maintain sinus rhythm. Age (p=0.045), significant mitral regurgitation (grade ≥ II/IV; p=0.026) and left atrium diameter >45mm (p=0.022), risk factors for AF recurrence described in literature, constituted predictors of RaM strategy choice. Regarding antithrombotic treatment, by virtue of ACS, the majority of P went home medicated with double antiplatelet therapy (100% with acetylsalicylic acid and 97.6% with clopidogrel). Additionally, anticoagulant therapy was introduced in 66.6% P oriented to RaM and 18.0% oriented to Rym. P submitted to RaM strategy that did not receive oral anticoagulants had a higher mortality in follow-up when compared to those who did receive (p=0.049). Anticoagulant therapy did not show any benefit in the P submitted to Rym. The RaM strategy was associated with higher mortality, when compared to Rym (p=0.001).

Conclusion: nAF diagnosed in the context of acute myocardial ischemia and with less than 48 hours of evolution is, in majority of cases, possible to revert to sinus rhythm. In this study, there was a tendency to the superiority of RyM over RaM and of anticoagulant therapy in the last group (results of univariate analysis). To validate these conclusions, randomized trials evaluating effects of RyM and RaM strategies, antithrombotic and antiarrhythmic management should be designed and executed.

P2720 | BEDSIDE
Acute coronary syndrome with prolonged hospitalization

Purpose: To determine the clinical characteristics that influence hospital length of stay in patients with acute coronary syndrome. Methods: We examined a cohort of patients admitted consecutively to a university hospital with a diagnosis of unstable angina or acute myocardial infarction. We selected those that did not require coronary artery bypass surgery and analytically associated with length of stay (LOS) of 10 days or more using a logistic regression analysis. Results: Between January 2007 and December 2010, our hospital admitted 1912 patients with acute coronary syndrome. 1537 of these (age 64 (54-74) years, 70.3% male) were discharged during the study period. Of them received invasive management and the overall hospital mortality was 6.6%. Patients with a LOS of 10 days or more (corresponding to the 75th percentile, n=464 (30.2%) were older (68 (58-75) vs 63 (52-73) years, p<0.001), with higher prevalence of hypertension: 70.9% vs 59.7%, p=0.001; diabetes: 37.9% vs 31%, p=0.008; peripheral artery disease: 11.2% vs 5.9%, p<0.001; chronic obstructive pulmonary disease: 7.1% vs 4.1%, p=0.013) and more frequently had multivessel disease (56.7% vs 41.7%, p<0.001). The multivariable analysis showed that the presence of chronic kidney disease (OR 1.70; 95% CI 1.08-2.68, p=0.023), anemia at admission (OR 2.14; 95% CI 1.55-2.96, p<0.001), cerebrovascular disease (OR 1.84; 95% CI 1.04-3.24, p=0.035), presence of Q-wave infarction (OR 1.88; 95% CI 1.40-2.54, p<0.001), moderate or severe mitral regurgitation (OR 3.27; 95% CI 1.45-7.37, p<0.004), and age (OR 1.02; 95% CI 1.01-1.03, p<0.001) were associated with a longer income. Complete revascularization during the episode was associated with a lower risk (OR 0.64; 95% CI 0.46 - 0.89, p<0.008).

Conclusions: Prolonged hospitalization after an acute coronary syndrome is related to the presence of anemia, chronic renal disease and mitral insufficiency independently of other related patient comorbidity factors. Complete revascularization is a protective factor.

TRANSPLANT NEWS

P2722 | BEDSIDE
Prognostic impact of acute rejection episodes during the first year after heart transplantation on long-term post-transplant survival
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Purpose: Acute rejection (AR) is a major complication after heart transplantation (HT). It is more common in the first year following HT, a period in which infection and graft failure have a decisive impact on patient’s prognosis. Our aim was to evaluate the prognostic implications of first-year AR, and its implication on one-year-conditioned long-term survival.

Methods: Retrospective study of patients who underwent HT in our center between April 1991 and December 2012. Patients younger than 18 years and those with renal replacement therapy or retransplantation were excluded. AR was defined by any clinically relevant event leading to an intensification of immunosuppressive treatment that included intravenous therapy. One-year-conditioned long-term survival of patients with or without AR during the first post-transplant year was compared by means of the Kaplan-Meier method (univariable analysis) and the Cox’s proportional hazards method (multivariable analysis).

Results: 609 patients (83% male, mean age 54±12 years) were studied over an mean follow-up of 8.3 years. 373 patients (61%) had at least one AR episode during the first post-transplant year. 47.8% of patients died during the follow-up of those 61% died within the first year. Patients with AR had significantly reduced non-adjusted one-year-conditioned long-term survival (log rank p=0.019) than patients without AR (graph). After multivariable adjustment, the presence of AR during the first post-transplant year remained as an independent predictor of one-year-conditioned long-term mortality (HR 1.42; 95% CI 1.07-1.91).

Conclusions: AR during the first post-transplant year has a negative impact on one-year-conditioned long-term survival. Therefore it is critical to prevent rejection, something still unresolved.

P2723 | BEDSIDE
Echocardiographic assessment of left ventricular longitudinal function and rest for detection of significant coronary artery stenosis in heart transplant recipients
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Purpose: Cardiac allograft vasculopathy (CAV) and late graft failure (usually secondary to CAV) are the most common causes of death in long-term heart trans-
plant (HTx) recipients. Currently available non-invasive tests show low diagnostic value, therefore invasive coronary angiography (ICA) is frequently performed. Left ventricular longitudinal function parameters at rest may be abnormal in patients with significant coronary artery stenosis, which might be used to evaluation of CAV. The aim of this study was to estimate their diagnostic performance in HTx patients versus a reference standard of quantitative ICA.

**Methods:** We enrolled prospectively 87 consecutive patients (mean age 53.1±13.3 years, 75 men) at least one year after transplant, who underwent resting echocardiography, annual routine ICA and myocardial biopsy. Mean post-transplant time was 6.4±4.0 years. All studies were analysed conventionally and quantitatively using tissue Doppler and speckle tracking techniques. We evaluated regional and global myocardial tissue longitudinal displacement, velocity and strain parameters. A 50% or greater stenosis by ICA was considered significant. Results: ICA was performed in 45 (51.7%) patients. In 19 (21.8%) patients significant stenosis was detected, of whom 8 patients needed stent implantation. Segmental wall motion abnormalities in the standard echocardiography occurred in 13 patients. Speckle tracking was possible in 97.6% of 1350 selected segments from the 85 studies with technically adequate images. Analysis of all 18 left ventricular segments was possible in 69 (79.3%) patients. In multivariate regression analysis only post-systolic shortening index (PSSI), tricuspid annular systolic velocity (RV S') and post-transplant time remained independent predictors of significant stenosis. The area under the receiver-operating-characteristic curve was 0.85 for RV S' and 0.79 for PSSI (P<0.001). Sensitivity, specificity, positive and negative predictive value for significant stenosis detection (PSSI threshold ≥25%) was calculated as 89.5%, 93.9%, 81.0% and 96.9%, respectively. Diagnostic accuracy was 92.9%.

**Conclusions:** Among the left ventricular longitudinal function parameters only PSSI might be used to evaluation of CAV. Low PSSI virtually rule out significant stenosis due to CAV. Therefore assessment of PSSI might avoid a significant proportion of invasive coronary angiography studies in heart transplant recipients.

**P2724 | BEDSIDE**

Achieving eligibility for heart transplantation: the role of sildenafil in advanced heart failure patients with pulmonary vascular disease

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**Background:** Pulmonary hypertension (PH) is a frequent complication of chronic heart failure (HF) and elevated pulmonary vascular resistance (PVR) remains a major problem for heart transplant (HTx) candidates selection. In this setting, a simple therapy to modulate severe PH and allow HT without compromising patient outcomes would be of great value. Our aim was to (1) assess the effect of pre-HTx sildenafil administration on pulmonary hemodynamics before and early after HTx and (2) in long-term mortality after HTx in high-risk patients because of extensive pulmonary vascular disease.

**Methods:** We performed a monocentric, retrospective study including 236 consecutive patients who underwent HTx between November 2003 and December 2013. Thirty Group A) received sildenafil therapy due to the presence of PVD (extensive pulmonary vascular disease or PVR) and 206 patients (Group B) did not receive sildenafil due to the absence of PVD. Pulmonary hemodynamics were evaluated before sildenafil initiation in all patients, early after HTx during the first endomyocardial biopsy at 1 week and 1 year after HTx in both groups. Survival after HT was compared between the groups using the Log-Rank test.

**Results:** The mean age of group A was 54.1±11 years and of group B 53.8±13 years. Mean pulmonary arterial pressure (mPAP), systolic pulmonary pressure (sPAP), PVR and transpulmonary pressure gradient (TPG) were respectively 40.1±12 mmHg, 63.1±17 mmHg, 435±180 dyn s/cm² and 13.1±1 mmHg in group A before sildenafil. Regarding group B, these values before HTx were 29.1±10 mmHg, 45.1±15 mmHg, 254±183 dyn s/cm² and 9.9 mmHg. Early after HTx, no differences were found regarding sPAP - 40.2±7.9 mmHg in group A vs 36.5±11.5 mmHg in group B (p=0.1) and right ventricular end-diastolic pressure 7.9±5.8 mmHg vs 6.9±17 mmHg (p=0.5). One year after transplantation, group A sPAP was 32.4±6.3 vs 30.5±8.2 in group B (p=0.3). Survival after HT was similar between the groups. With a median follow-up of 35 months (range 28 - 87 months), 55 (40.5%) patients died in group A and 23 (11.2%) in group B. In group A we found significance PVR (p=0.05) and DPG (p=0.01). In group B, the right atrial pressure post HTx was significantly lower in the group with DPG <4 (p=0.05) as well as PVR (p=0.05). Despite the lack of statistical significance, we also found a favorable trend toward increased CO in the group with DPG >4.

**Conclusions:** Although patients treated with sildenafil had significantly worse pre-HTx hemodynamics markers, signaling for preexisting PVD, no differences were found after-HTx hemodynamic variables. These findings support the concept that sildenafil can rescue previously ineligible HTx patients due to severe, fixed PVD.

**P2725 | BENCH**

Bacteria and bacteriophages in the myocardium are related with resistance to pulse therapy in myocardial rejection

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**Purpose:** Cardiotropic bacteria and many viral DNAs were described in Dilated Cardiomyopathy (DCM). In previous study we found in DCM biopsies, human vi-
heart at the midatrial level and the bivacal technique (BC) with resection of the superior and inferior vena cavae, preserving the integrity of right atrium. BA technique has been associated with atrial dysrhythmias and sinus node dysfunction. BC technique has the advantage of atrial contractility and sinus node function, but this procedure takes longer to complete and prolongs ischemic time. Permanent pacemakers (PM) are generally indicated only for bradycardia that does not resolve and is associated with symptoms. PM implantation is required after orthotopic HTX in 4-29% of transplant recipients. The aim of this study is to describe changes in spectrum of clinical indications for posttransplant PM placement over the years. This study reflects this change with the increase in evidence of HTX.

Methods: The HTX database, medical records and pacing database/records were reviewed for all patients undergoing de novo orthotopic HTX (n=934) at our institution between January 1984 and December 2013. BA surgical technique of HTX was used until 1993. Since 1993 BC technique has been employed at our institution in all patients.

Results: A total of 48 patients (5.3%) received a PM after HTX. Mean age was 54±8 years, 10 patients were females. Clinical indication for PM was sick sinus syndrome in 19 cases (25%), in 4 pts with atrial bigeminy. AV sequential block was an indication for PM in 37 pts (77%). In 30 of them, PM was implanted early after HTX (7-49 days). In remaining 2 pts (4%), the reason for PM implantation was syncopa and bundle branch block. BA surgical technique was used in 89 pts, 4 of them (4.5%) received PM, all of them for clinical indication of sick sinus syndrome. BC technique was performed in 465 pts, 44 of them (3.5%) were indicated for PM placement, almost all of them for AV block.

Conclusions: In our study, PM was implanted after HTX in 5.3% pts. With bivacal surgical technique of HTX the need for pacing has not changed, but in the spectrum of clinical indications for PM placement anteroinferior block became predominant.

P2728 | SPOTLIGHT
Vectorcardiographic predictors of pediatric heart transplant acute graft rejection
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Introduction: The vectorcardiographic (VCG) parameter, the spatial QRS-T angle of vectorcardiograms has been postulated to be predictive of arrhythmias in adults with ischemic heart disease. We hypothesized that the spatial QRS-T angle and its vector components (tested along with QTc measurements) would be associated with endomyocardial biopsy (Bx) proven moderate acute cellular rejection (ACR) in a pediatric population of orthotopic heart transplant (OHT) recipients.

Methods: A blinded, retrospective evaluation of patients (pts) with available Bx data was performed. Resting 12-lead electrocardiograms (ECGs) done on the day of Bx and clinical data were collected. The following parameters were calculated: QTc, spatial QRS-T angle, the principal QRS-axis and T-wave vector components (root mean square of the X, Y, and Z components of the QRS and T-wave complexes, respectively). Student t-tests and the Mann-Whitney U test were used as appropriate to assess significant differences between pts with and without biopsies (p<0.05).

Results: There were 97 biopsies reviewed in 83 pts. The mean age was 13.9±5.0y, the median time from transplant was 8.0 yr ([Q 3.2-11.9], and 52% were male. Pre-OHT diagnosis was cardiomyopathy in 50 (52%), congenital heart disease with pre-capillary component: hemodynamic and functional impact in 9 cases (19%); in all 4 pts with biatrial technique. Atrioventricular valve surgical technique of HTX the need for pacing has not changed, but in the spectrum of clinical indications for PM placement anteroinferior block became predominant.

P2729 | SPOTLIGHT
Phosphodiesterase-5 inhibitor in pulmonary hypertension due to left heart disease with pre-capillary component: hemodynamic and functional impact
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Introduction: Pulmonary hypertension (PH) in chronic heart failure results from passive backward transmission of high left heart pressures, frequently associated with a component of pulmonary vascular disease (PVD), defined by an increase in vasomotor tone and/or obstructive remodeling of vessels’ wall. PH carries a poor prognosis and may preclude heart transplant in end-stage cardiac disease. Phosphodiesterase-5 inhibitors are considered as a rational choice of therapy in PH, however its value in group 2 PH is still controversial. This study evaluates the clinical and hemodynamic utility of sildenafil in patients (pts) with advanced heart failure (AHF) and PH with a pre-capillary component.

Method: Retrospective unincident study of pts with AHF referred for heart transplant over the past 10 years. Clinical, laboratory and hemodynamic (right heart catheterization) data were collected from pts with out-of-proportion PH, in whom sildenafil was prescribed “off-label”.

Results: 55 pts had complete hemodynamic evaluation before and during treatment with sildenafil. Mean age was 45±17 years and 69% were male. The majority had severely compromised functional capacity, half being in NYHA class IV; peak VO2 was 15.1 (IQ 12.4 – 17.3) mL/kg/min. Median values of BNP were significantly elevated (540 [IQ399–1035] pg/dL). Before the treatment, hemodynamic parameters of patients (systolic blood pressure [SBP] 46±11 mmHg, mean pulmonary capillary wedge pressure [PCWP] of 27.48±8.89 mmHg, cardiac output (CO) of 3.19±0.84 L/min and high pulmonary vascular resistance (PVR) 547.25±267.39 dynes s-1cm-5). After 3 months (median) of therapy patient’s functional capacity, BNP levels and hemodynamic profile improved significantly. By then, only 19.7% of pts were still in NYHA functional class IV. BNP reduced on average 6% (p=0.046) and mean peak VO2 increased to 17.8 mL/kg/min (+17%, p=0.048). Regarding hemodynamic parameters, there was a mean reduction of mPAP of 21% (p<0.001) and of PCWP in 22% (p<0.001), an increase of CO in 24% (p<0.01) and a reduction of 39% in PVR (p<0.001); these changes were most visible in pts with a transpulmonary gradient (TPG) >12 mmHg. No significant side effects were reported with the use of sildenafil, namely systolic arterial pressure decrease during treatment.

Conclusion: Sildenafil improved significantly the clinical and hemodynamic profile of pts with advanced heart failure and PH with a reactive component, and also showed to be safe. Its use may be of particular interest in rescuing pts with established PVD for eligibility for heart transplant.

P2730 | BEDSIDE
Superior rejection profile during the first 24 months after heart transplantation under tacrolimus as baseline immunosuppressive regimen
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Background: The use of tacrolimus in heart transplant patients increased during the last decade. Aim: In this retrospective study, we evaluated the effects of a tacrolimus (TAC) based immunosuppressive therapy regarding rejection profile in comparison to a Cyclosporine A (CsA) based regimen in patients after heart transplantation (HTx).

Patients: The data of 233 patients were evaluated. Patients were followed until HTx. Primary end-point was time to first rejection requiring therapy. In all patients routine follow-up at our Center was mandatory.

Results: No statistical significant differences regarding recipient age, donor age, recipient gender, ischemic time, and diagnosis leading to HTx were found between the two groups (all p>0.05). Time to first biopsy proven rejection requiring therapy was significantly longer in the TAC group (logrank analysis, p=0.0003) in all patients still on baseline immunosuppressive schedule two years after HTX (n=150). Likewise, in the remaining patients, who underwent a change in immunosuppressive regimen also a significant longer time to first biopsy proven rejection was observed in the TAC group (logrank analysis, p=0.012) compared to the CsA group. Furthermore subgroup analysis in the TAC subgroup showed a longer time to biopsy proven rejection under prolonged release TAC compared to conventional TAC, however the level of statistical significance was not met (logrank analysis, p=0.1736).

Conclusion: Our study demonstrated that a TAC based primary immunosuppressive therapy is superior to a CsA based immunosuppressive regimen in patients after HTx regarding time to first biopsy proven rejection requiring rejection.

P2731 | BEDSIDE
The impact of human leukocyte antigen matching on rejection after heart transplantation
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Background: The main antigenic stimulus for allograft rejection is the major histocompatibility complex (MHC) encoded human leukocyte antigen (HLA) system. HLA matching is not considered in current allocation policies in heart transplantation. The aim of our study was to assess the impact of HLA matching on rejection after HTx. Additionally, we compared the rejection profile of patients who received a HTx after a heart-lung transplantation (HLTx).

Patients and methods: Forty patients transplanted between November 2011 and July 2013 were analyzed retrospectively. The shortest follow-up time was 6 months. The mean follow-up time was 14.17±5.65 months (6-26 months). Immunosuppressive therapy consisting of TAC, mycophenolate mofetil and corticosteroid. HLA mismatches on the major antigen loci HLA-A, -B and -DR were analyzed.

Results: Thirty-seven HLA matching were observed in 20 patients (50%). Five patients matched only at the DR locus. Thirty-two patients were treated with HTx after a HLTx. Seven patients were treated with TAC after a HLTx. The majority of patients received a HTx after a HLTx were treated with ATG, corticosteroid and mycophenolate mofetil. Maintenance therapy was performed using tacrolimus, mycophenolate mofetil and corticosteroid. HLA mismatches on the major antigen loci HLA-A, -B and -DR.
were calculated (zero to six mismatches). All patients were routinely monitored for cellular rejection with scheduled endomyocardial biopsies. 

**Results:** During the follow-up period 11 patients (27.5%) suffered from grade 1R acute rejection. Fifteen patients (37.5%) had 1 HLA-DR mismatch, while 4 patients (10%) were with-out HLA-DR mismatches, and 1 patient (2.5%) had 2 HLA-DR mismatches. We found a significant positive correlation between the number of HLA-DR mismatches and grade 2R acute rejection (p<0.03). HLA-DR identical recipients didn’t have grade 2R cellular rejection during the follow-up period.

**Conclusions:** The investigation of HLA matching can be useful clinical parameter to predict rejection episode after heart transplantation. Patients with better HLA compatibility might require lower immunosuppressive therapy.

**P2733 | BEDSIDE**

Long-term experience with heart transplantation in children and patients with congenital heart disease


**Purpose:** The purpose of this study was to determine the correlation between conventional pacemaker (PM) lead impedance and degree of congestion at the time of heart failure (HF) hospitalization. Intrathoracic impedance, measured using specialist equipment, falls, as the amount of conductive intrathoracic fluid increases with pulmonary congestion. We hypothesized that monitoring of conventional PM lead impedance may also provide an early warning means of congestion.

**Methods:** Twenty-four patients with NYHA class III/IV HF and previously implanted PM for bradycardia indications, were admitted to our department with acute decompensation of chronic HF. All enrolled patients had signs of pulmonary congestion, increased jugular venous pressure and peripheral edema. The right JVP was assessed at admission and before discharge with the patient reclining at 450.

The lead impedance was measured in VVI mode with unipolar pacing at 5V with the PM analyzer. A pre-discharge value of PM impedance was established as the “reference impedance” and used to quantify the magnitude of any impedance change. At 3 month follow-up, PM impedance and a JVP were measured.

**Results:** PM impedance correlated with changes in clinical congestion assessed by JVP. Impedance was low on admission (mean value 340±40 Ohms) and increased after intensive diuresis (mean value 420±50 Ohms). JVP was high (mean value 20cm H2O), and decreased after treatment (mean value 14cm H2O). During the 3 month follow-up visit the PM impedance was comparable to the reference impedance in most patients, mean difference±20 Ohms, whereas 3 patients who had worsening HF, had lower than reference impedance (mean decrease 60 Ohms). This was considered an “early warning” and we admitted these patients to hospital, where impedance up went again after treatment. A major finding in this study was the report preliminary experience between conventional PM lead impedance and clinical fluid status evaluation.

**Conclusions:** The findings from this study suggest that monitoring of PM impedance at regular intervals during HF therapy may provide quantitative information on the severity of volume overload and a warning sign of impending HF decompensation. Further studies are needed to determine whether such an early warning can facilitate preemptive therapy to reduce hospital admissions.

**P2734 | BEDSIDE**

Pediatric ventricular assist device: a single centre preliminary experience

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**Objective:** Pediatric ventricular assist device (VAD) is currently used as mechanical circulatory support device for adolescents, infants and small children with advanced heart failure. We report our preliminary experience (a third level centre of Paediatric Cardiology and Cardiac Surgery) with VAD.

**Methods:** Between April 2009 and February 2014, 8 children (4 male and 4 female) followed in our Department of Paediatric Cardiology underwent pediatric VAD implantation at the Cardiac Surgery Division of our hospital. The diagnosis was myocarditis in 6 patients, idiopathic dilated cardiomyopathy in a single case and heart failure secondary to valve disease in one of them. Two cycles of i.v. inotropic therapy (dobutamine and levosimendan) were undertaken before im-

**Figure 1**
plantation. In addition, all patients underwent imaging evaluation (including cardiac Magnetic Resonance Imaging (MRI) in 3 patients), cardiacthe- ridization, endomyocardial biopsy (EMB) and viral genome PCR at VAD implantation.

Results: The median age at implantation was 8.8 years (2 to 15 years), the mean weight was 40 kg (13 kg to 64 kg), and the median support time was 121 days (5-459 days). Four pts received a BIVAD and 4 pts a LVAD. In three pts, MRI showed diffuse subependymal enhancement without signs of intracerebral and interstitial edema, capillary leakage and hyperemia. On the other hand, EMB showed diffuse fibrotic replacement without signs of active inflammation in all pts while at PCR only in one case a viral etiology (CMV) was revealed. Out of our 8 pediatric pts, 6 were bridged to heart transplantation, 1 died on support, and 1 is still waiting for heart transplantation. After heart transplant, 3 pts needed an ExtraCorporeal Membrane Oxygenation (ECMO), 3 pts had chest wound infection and one had hyperacute rejection and bleeding problems. These complications occurred only in patients that underwent implantation in I-II INTERMACS level, while patients implanted at an early stage had no complications.

Conclusions: In agreement with literature, our experience confirmed that paedi- atric VAD could provide satisfactory and safe circulatory support for children with end-stage heart diseases. Further studies are needed to better define the prog- nostic impact of timing of device implantation and choice between univentricular vs biventricular support in pts with end stage disease.

P2737 | BEDSIDE
Preoperative hemodynamic and echocardiographic predictors of right ventricular failure after left ventricular assist device implantation

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Objectives: Although preoperative prediction of Right Ventricular Failure (RVF) after Left Ventricular Assist Device (LVAD) implantation is a frequently laboured entropy, there is still no consensus about any hemodynamic or echocardiographic pa- rameter. In this trial, we aimed to detect new pre-operative hemodynamic and echocardiographic parameters in order to predict RVF after continuous flow LVAD implantation.

Methods: From March to November 2013, 26 continuous flow LVAD implanted patients (23 male,3 female; mean age 49±12) were included in our single cen- ter,prospective,observational study,Patients’ pre-operative Right Heart Catheteri- sation (RHC) and echocardiographic findings were evaluated. Post-operative RVF was defined as inotrophy dependence for more than 14 days and/or need for RVAD implantation.

Results: 15 patients included in the study had ischemic and 11 patients had non-ischemic etiology.22 patients had HeartWare and 4 patients had HeartMate II. Functional classes were defined according to INTERMACS classification. 3 patients were in INTERMACS I-I,18 patients were in INTERMACS III-IV and 6 patients were in INTERMACS V-VII class. 3 patients (11%) had RVF. In 2 patients in INTERMACS I-I and 1 patient in INTERMACS III-IV, RVF was stated.No RVF was developed in INTERMACS V-VII group. Among echocardiographic data; low TAPSE (p=0.01), low right ventricular outflow tract-SE (RVOT-SE) (p=0.04) and increased RV diameter (p=0.01) were found statistically signifi- cant to be associated with RVF. Among RHC findings increased RAP (p=0.04), di- astolic RV pressure (RVdp) (p=0.04) and low diastolic pulmonary gradient (DPG) (p=0.01) were found statistically significant to predict RVF.

Conclusions: Increased RAP, RVpdp, low DPG, low TAPSE, FAC, RVOT-SE mea- surements and increased RV diameters were detected to predict RVF. Despite our small study population, we think that DPG, RVOT-SE and other parameters found to be associated with post-operative RVF will be a pathfinder for bigger prospec- tive trials with larger study populations.

P2738 | BEDSIDE
New generation left ventricle assist device does not affect microvascular endothelial tone regulation and vWF production

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Purpose: Left Ventricular Assist Device (LVAD) is a promising new therapy for patients with advanced heart failure. Previous studies suggest that continuous blood flow impairs endothelial function. Effects of last generation LVAD device on microvascular endothelial function, endothelial nitric oxide (NO) bioavailability and vWF metabolism are not known.

Methods: We compared LVAD-supported patients (n=13) with age/BMI matched non-supported patients (n=13) with chronic heart failure (CHF, n=13) and healthy subjects (Control, n=15). All patients were implanted with a HeartWare® LVAD. Skin microvascu- lar endothelial function was assessed with Laser Doppler Imaging and hyperemic tests using acetylcholine (Ach) and sodium nitroprusside (SNP) isohypoxia. NO-mediated vasodilatation was further evaluated by comparing heating hyperemic response in skin area pretreated either by a specific NO-synthase inhibitor (L-NAME) or a control saline solution. Monomeric and high molecular weight multi- meric (HMWM) vWF antigens and vWF activity were also measured.

Results: Compared to control, CHF patients had both reduced Ach and SNP- induced vasodilation (all p<0.05; Fig. 1), whereas LVAD patients have no signifi- cant differences in Ach and SNP responses. Endothelial NO bioavailability did not differ between LVAD, CHF and control group. Compared to CHF, LVAD did not affect vWF endothelial production or vWF activity. However, we observed in 2 LVAD-supported patients a loss of HMWM vWF and no abnormality in other groups.

P2739 | BEDSIDE
How long is too long? Extended biventricular assist device support as a bridge to heart transplantation in a low organ donation environment

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Purpose: Low organ donation combined with delayed referral of advanced-stage cardiomyopathy patients necessitates biventricular assist device (BiVAD) support for extended periods of time. Reliable devices and close patient follow-up increase the survival likelihood. We report our experience with the Berlin Heart Exact Bi- VAD.

Methods: Sixty-three biventricular Berlin Heart Excort devices have been im- planted since 2004. Patients’ ages ranged from 11 to 60 years (median age 35 years). Diagnoses included dilated (74.5%), ischemic (17%) and others (8.5%) cardiomyopathies (fulminant myocarditis, restrictive cardiomyopathy, Amyloidosis,ARVC). All patients presented in severe biventricular failure (intravascular in- otropes, 40; ventilated, 10; IABP, 35; mean: CI 1.9 L/min/m2; CVP 19 mmHg; total bilirubin 3.75 mg/dl; Nf-proBNP, 25,500 pg/ml). Two patients needed a Bi- VAD after left ventricular assist device support of 439 and 295 days, respectively. Anticoagulation consisted of heparin, Vitamin K antagonist, aspirin, dipireidamole and clopidogrel.

Results: Thirty, day 180, and 1 year after implantation (excluding endstage liver disease) survival was 99.5%, 88.2%, and 82%, respectively.Thirty-two patients were bridged and nine are ongoing. Mean time on support was 681 days and 58 out of 63 patients with adult-sized pumps were discharged home with a mo- bile driver.Thirty patients exceeded 2 years of uncomplicated support before they were heart transplanted. Five patients were still on support at 3 years after transplantation. One patient with renal failure and dialysis dependence lives at home 3.5 years after implantation. Complications included infection (n=15), bleeding re- quiring reexploration (n=5), and thromboembolic events (n=10). Patients died, 1 of an accidentally ruptured canna (after 365 days), 6 of sepsis, 5 of multiorgan system failure.

Conclusions: Reliability of components and strict utilization of patient-care pro- tocols leads to excellent survival in this extremely sick population. Meticulous multi-disciplinary management by experienced personnel is essential.

P2740 | BEDSIDE
Pre-operative hepatic dysfunction could predict postoperative mortality and morbidity in patients undergoing open-heart surgery; utilization of the MELD scoring system


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Background: Patients who require open-heart surgery frequently suffer from hepatic dysfunction due to the underlying right ventricular failure. The Model of End-stage Liver Disease (MELD) score allows risk-stratification of patients un- dergoing major cardiac and non-cardiac surgery.

Purpose: The aim of this study is to evaluate the impact of pre-operative MELD score on postoperative outcomes following open-heart surgery.

Methods: We analyzed 532 consecutive patients (67.3% male, mean age 67.8±12.9 year-old) undergoing open-heart surgery between January 2013 and October 2013 at our institution. Associations between liver dysfunction estimated by the MELD score and post-operative clinical courses were analyzed.

Conclusion: MELD therapy tends to normalize microvascular endothelial tone regulation impairment present in CHF population and does not affect endothelial NO bioavailability or endothelial regulation of vWF. However, LVAD is associated with a loss of HMWM vWF, which could favor bleeding complications.
Results: The mean value of the MELD score obtained from the total cohort was 9.4±4.3. Patients with high MELD scores (>12) were associated with longer intubation time (24.9±6.05 vs. 12.3±26.8 hours, p=0.0087), longer length of stay in the intensive care unit (3.7±4.5 vs. 2.1±2.5 days, p<0.0001) and longer hospital stay (16.8±15.9 vs. 13.8±11.6 days, p=0.0289) as compared to those with low MELD scores (<12). The MELD score was correlated with the total length of stay in hospital (r=0.201, p<0.0001). Multivariate analysis revealed that the MELD score was independently associated with >30 days of stay in hospital (odds ratio 1.08, p=0.0495), which was predictive of >30 days post-operative stay with a sensitivity of 71.9% and a specificity of 51.7%. Regarding mortality and morbidity, high MELD score was associated with higher mortality rate (>3.75 vs. 0.82%, p=0.0337) as well as higher incidences of atrial fibrillation (37.5 vs. 34.0%, p=0.0013), hemodialfiltration or hemodialysis (43.4 vs. 4.9%, p<0.0001) and stroke (>4.0 vs. 0.9%, p=0.0020) after surgery. The Kaplan–Meier analysis showed lower survival rates in patients with a MELD score >12 as compared to those with a MELD ≤12 (90 >days survival, 95.9 vs. 99.4%, log-rank p=0.0125).

Conclusion: Assessment of liver dysfunction using the MELD scoring system provides additional risk information and is useful for predicting post-operative mortality and morbidity in patients undergoing open-heart surgery.

P2741 | BEDSIDE Outcomes of the arterial switch operation for transposition of the great arteries
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Background: The arterial switch operation (ASO) is currently the standard surgical procedure for transposition of the great arteries (TGA). The purpose of this study is to evaluate the early and late outcomes of ASO and the incidence of and risk factors for transcatheter or surgical re-intervention.

Methods: A total of 223 Patients (162 boys and 61 girls), with median age of 29 days (3-1074) and mean weight of 3.68 kg (2.1-15 kg) at operation, underwent ASO in our institution from 1998 to 2012. Patients were divided into three groups according to the indication for the ASO: group A, TGA with intact ventricular septum (n=135); group B, TGA with ventricular septal defect (VSD) (n=72); and group C, Taugss-Bing anomaly (TBA) (n=16). Balloon atrial septostomy (BAS) were done in 160 (72%) patients before the surgery. 64 (28.7%) patients had abnormal coronary artery patterns. 16 (7.2%) patients had aortic anomaly which included coarctation of the aorta (CoA) (n=12, 5.4%), interrupted aortic arch (IAA) (n=1, 0.4%), and CoA with right aortic arch (RAA) (n=1, 0.4%). The median follow-up period was 5.81 years (range 0 to 14.06 years). Statistical analysis was performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL USA).

Results: Early mortality included one patient from group A who had an extracorporeal membrane oxygenation (ECMO) implanted intra-operatively. Late mortality contains two patients who died after discharge on the twenty-fifth and thirty-eighth postoperative day. Pulmonary stenosis (PS) developed in 44 (20%) patients, of which, 17 (39%) patients underwent re-interventions. The median time to re-interventions was 4.68 years (range 0 to 14.06 years). Re-interventions (n=14%) included balloon angioplasties (n=16, 7%), reoperations (n=5, 2%) and a combination of both (n=10, 5%). Balloon angioplasties were performed in 7 (5.2%), 5 (6.9%) and 4 (25%) patients in groups A, B and C, respectively. Two reoperation each was performed in groups A and B. One reoperation was in group C. Balloon angioplasties and reoperations was performed in 3 (2.2%), 5 (6.9%) and 2 (12.5%) patients in groups A, B and C, respectively. Uni-variate Cox analysis identified TBA (p=0.001), VSD (p=0.008), pulmonary stenosis (p<0.001), presence of aortic anomalies (p=0.003), BAS (p=0.046) and abnormal coronary artery (p=0.03) as potential risk factors for re-intervention.

Conclusion: The arterial switch operation can be performed with excellent outcomes. However, a large population of patients requires re-intervention. A regular life-long cardiac follow-up is, therefore, recommended.

P2742 | BEDSIDE Single center experience with heartware left ventricular assist device: outcome in high risk patients
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Purpose: To present our experience with the HeartWare ventricular assist device (LVAD) implantation at our center and its clinical outcome in critically sick patients (pts).

Methods: Outcome of HeartWare VAD implantations performed at single institution from 01.2010- 02.2014 was studied. The study design was a retrospective analysis of the prospectively collected data.

Results: 58 pts with a mean age of 55±12 years were included. Fifty pts were male (86%). The preoperative INTERMACS profile of the pts was I 26 (45%), II 7 (12%), III 7 (12%) and IV 18 (31%). Twenty-two pts (38%) were on extracorporeal membrane oxygenation (ECMO) before VAD implantation. The median duration of VAD support was 204 days (2-1250 days). With a total support duration of 37 days post, Kaplan –Meier analysis revealed a survival of 77%, 74% and 74% at 180 days, 1 year and 2 years respectively. Nineteen pts (33%) were successfully bridged to heart transplantation. Device explanation was performed in four pts (7%) after recovery of the left ventricle. Postoperative complications included right heart failure in 23 pts (40%), respiratory failure in 19 (33%), renal failure in 18 (31%), gastrointestinal bleeding in 14 (24%), 11 reperatation for bleeding (19%), 8 neurologic dysfunctions (14%), 7 driveline infections (12%), and 7 events (12%) of pump thrombosis. A significantly lower survival rate and higher postoperative complications were observed in pts with preoperative ECLS (p<0.005) (Fig. 1).

Conclusions: Considering the sick pt population included in this study, the outcomes following HeartWare VAD implantation is very satisfactory with survival to 180 days and/or transplantation of 77%. The outcome in pts with preoperative ECLS is significantly lower and associated with higher postoperative complications.

P2743 | BEDSIDE Left ventricle endocardial leads for cardiac resynchronization therapy. Long term follow up

Aim: Aim of the study is to analyze long term effects of biventricular pacing in patients with cardiac resynchronization devices where left ventricle leads were placed endocardially by using transseptal or transapical approach.

Methods and materials: 136 cardiac resynchronization devices were implanted from 11 January to 1 September in our Centre, 80 CRT – D devices and 56 CRT – P. In 13 patients of this group left ventricle lead was placed alternatively due to features of coronary sinus – 3, or high thresholds in target branches of coronary sinus – 4, or diaphragmatic nerve stimulation – 3, continuous lead dislodgement from venous system of heart - 3: whether by using left thoracotomy – 3, or thoracoscopic approach – 1, or transapical approach – 6, or transapical approach – 3.

Endocardial left ventricle lead placement was performed by using transseptal or transapical approach. All left ventricle endocardial leads (9) were implanted in patients with permanent atrial fibrillation and warfarin was already administered in this cohort of patients before CRT-P/D implantation. All patients underwent TEE 24 hours before the procedure to exclude the presence of thrombus in left chamber.

Results: All left ventricle leads were implanted successfully from the first attempt without major complications. Acute thresholds for the left ventricle leads were in normal range. No thromboembolic events were revealed in these patients during follow up period. No dislodgements or other left ventricle lead failure were diagnosed.

According to echo 3D strain examination this cohort of patients had more homogeneous and effective contractile function of left ventricle when compared with cohort of patients with routine technique of left ventricle lead implantation.

Conclusion: 1) Alternative methods of endocardial left ventricle lead placement could be methods of choice in patients with previous unsuccessful attempts of lead placement into the branch of coronary sinus. 2) Left ventricle endocardial lead placement is safe and gives an operator a possibility to choose the region of lead implantation. 

P2744 | BEDSIDE The variation of left ventricular strain after aortic valve replacement by three-dimensional speckle tracking echocardiography

Objective: To investigate the variation of left ventricular strain by three-dimensional speckle tracking echocardiography in patients underwent surgical aortic valve replacement (AVR)

Methods: Twenty patients with severe aortic stenosis (AS) and 16 patients with severe aortic incompetence (AI) were enrolled. All patients underwent AVR with LVEF>55% before the operation. Global longitudinal strain (GLS) and global circumferential strain (GCS) were evaluated by three-dimensional speckle tracking echocardiography before AVR, 1 week and 1 month after AVR.
**HEART FAILURE MANAGEMENT**

**P2745 | BEDSIDE**

Predictors of hospital readmission for sternal wound infection after coronary artery bypass grafting surgery

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**Introduction:** Readmission after surgery is one of the indicators for quality of care and resources utilization. Sternal wound infection after coronary artery bypass grafting surgery (CABG) in patients with median sternotomy is a frequent cause of hospital stay and the cost. The aim of this study is to investigate the predisposing factors for hospital readmission because of sternal wound infection in order to develop strategies to minimize this problem.

**Patients:** A retrospective, multi-center, prospectively collected data base included all patients admitted for first time, isolated Coronary artery bypass grafting surgery during 3 years period from May 2007 to May 2010. Redo patients and combined surgery are excluded from the study. Univariate and multivariate analysis were used to identify incidence and Predictors of Hospital readmission for sternal wound infection after discharge following coronary artery bypass grafting surgery are identified.

**Results:** Out of 2121 patients who had first time isolated CABG in 3 years period; 721 patients (34%) were discharged for sternal wound infection. Those patients represent 57.5% of readmission for any reason. The age of the patients who required admission was 64.97±1.93 compared with 62.32±10.21 for those who did not require readmission (p<0.02); Female are more likely need readmission. Predictors for readmission for sternal wound infections are care score (odds ratio: 1.03 CI: 63.170) BIT A (odds ratio: 1.40 CI: 0.64-3.05) BMI (odds ratio: 1.03 CI: 0.97-1.09) Gender (odds ratio: 0.26 CI: 0.13-0.52) Age years (odds ratio: 0.95 CI: 0.91-0.98) and hypertension (odds ratio: 1.07 CI: 0.30-3.71).

**Conclusion:** This study showed that although readmission rate for sternal wound infection is small (3.5%), but it represented more than half of the rate of readmission. Women have a higher risk of readmission. Further large scale studies are needed to develop strategies to minimize this problem.

**P2746 | BEDSIDE**

Outcomes of the arterial switch operation for transposition of the great arteries for coronary anomaly

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**Background:** The arterial switch operation (ASO) for transposition of the great arteries (TGA) in patients with coronary anomalies is associated with an increased risk of coronary events and mortality. The purpose of this study is to evaluate the early and late outcomes of ASO and the incidence of and risk factors for transcatheter or surgical re-intervention.

**Methods:** A total of 64 patients with TGA and coronary anomaly (47 boys and 17 girls), with median age of 29 days (3-364) and mean weight of 3.62 kg (2.1-1.67 kg) at operation were included in our institution from 1998 to 2012. Patients were divided into three groups: group A, TGA with intact ventricular septum (n=33); group B, TGA with ventricular septal defect (n=22); and group C, Tauscott-Bing anomaly (TBA) (n=9). Balloon atrial septostomy (BAS) was performed in 38 (59%) patients before surgery. 6 (10%) patients had an aortic anomaly which included coarctation of aorta (COA) (n=5), 8% had mitral valve abnormalities (MV) and 1% had isolated aortic arch (IA) (n=1). Secondary thorax closure was performed in 36 patients (56%). The median follow-up period was 6.41 years (range 0.10 to 14.25 years). Statistical analysis was performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL USA).

**Results:** There was no early mortality. Late mortality included one patient from group B who died after discharge on the thirty-eighth postoperative day. Pulmonary stenosis (PS) developed in 16 (25%) patients, of which 9 patients underwent re-interventions. The median time to reintervention was 4.37 years (range 0.10 to 14.50 years). Re-interventions (n=10; 16%) included balloon angioplasties (n=6, 9%), re-operation (n=2, 3%) and a combination of both (n=6, 9%). Balloon angioplasties were performed in 4 (12%), 2 (9%) and 2 (22%) patients in groups A, B and C, respectively. One reoperation each was performed in groups A and C.

A combination of balloon angioplasty and reoperation was performed in one (3%), 3 (14%) and 2 (22%) patients in groups A, B and C, respectively. Univariate Cox analysis identified TBA (p=0.03), preoperative BAS (p=0.05), presence of aortic anomalies (p=0.01), single coronary artery (p=0.025) and PS (p=0.006) as potential risk factors for re-intervention. However, only the latter two (p=0.03 and p=0.008, respectively) were the predictors of late re-intervention as confirmed by Cox multivariate analysis.

**Conclusion:** The ASO in patients with coronary anomalies can be performed with excellent outcomes. However, a large population of patients requires reinterventions. A regular life-long cardiac follow-up is, therefore, recommended.

**P2747 | BEDSIDE**

Beta-2 adrenergic receptor gene polymorphism Gln27Glu is associated with the clinical status, heart rate and blood pressure history in chronic heart failure patients

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**Purpose:** Prior studies have shown that β-adrenergic receptor (β-AR) single nucleotide polymorphisms (SNP) affect outcomes in patients with heart failure and after acute coronary syndrome. Our aim was to estimate relationship of β2-AR gene polymorphism Gln27Glu with severity of clinical symptoms, renal and cardiovascular function in patients with chronic heart failure.

**Methods:** β2-AR gene polymorphism Gln27Glu was genotyped in genomic DNA from blood isolated from 66 CHF pts with 1-I NYHA functional class (FC) without primary renal, endocrine, autoimmune and oncological diseases. We analysed (p=0.03 and p=0.008, respectively) were the predictors of late re-intervention as confirmed by Cox multivariate analysis.

**Results:** 25.8% of pts had Glu/Glu, 45.5% - Glu/Gln, 28.8% - Gln/Gln genotype. The carriers of the Gln/Gln genotype had more severe CHF (mean NYHA FC in the Glu/Glu was 2.5±0.5, in the Glu/Gln- 2.6±0.6, in the Gln/Gln - 2.8±1.1, p=0.003). The duration of AH in anamnesis was longer in the Glu/Glu genotype (14.6±2.6, 10 (1-14) and 0 (0-7) years in the Glu/Glu, Glu/Gln and Gln/Gln, respectively, p<0.028). 57.7% of pts had sinus rhythm, others – permanent atrial fibrillation without differences within genotype groups. Minimal 24-hour ECG heart rate was lower in the Glu/Glu genotype (40 (36-42), 47 (43-49) and 49 (44-61) per minute in the Glu/Glu, Glu/Gln and Gln/Gln, respectively, p=0.015). Maximal 24-hour ECG RR interval was longer in the Glu/Glu genotype (2248 (1736-2960), 1760 (1624-1888) and 1564 (1488-1728) mc in the Glu/Glu, Glu/Gln and Gln/Gln, respectively, p<0.05). No association was found between Glu27Gln SNP and some selected 24-hour ECG parameters (X2-monitoring, mean normal work for hst, UEF, transmural E/A and E/Ea ratio, e-GFR and UAE in the Glu/Glu, Glu/Gln and Gln/Gln genotype groups.

**Conclusions:** We found that the Gln/Gln genotype of β2-AR gene is associated with severity of CHF and the Glu/Gln genotype – with lower trend for heart rate and longer duration of atrial hypertension before CHF development.

**P2748 | BEDSIDE**

Association of plasma HSP 27 level with severity and prognosis in patients with heart failure secondary to ischemic or dilated cardiomyopathy

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**Background:** Heat shock protein 27 (HSP 27) is a member of the heat shock protein family member, which is induced by a variety of stressors and functions as chaperone in the heart. Recently, circulating HSP 27 was reported to be associated with cardiovascular disease such as acute coronary syndrome and atherosclerosis. However, it remains to be determined whether circulating HSP 27 level can predict cardiac prognosis in patients with chronic heart failure (CHF).

**Methods and results:** We measured plasma HSP 27 level in consecutive 148 patients with CHF due to ischemic or dilated cardiomyopathy, and 24 control subjects. Plasma HSP 27 level was significantly higher in CHF patients (14.5±7.6 ng/ml) than in those with low HSP 27. Furthermore, we observed a positive correlation between plasma HSP 27 level and the NYHA functional class. Plasma HSP 27 level was significantly higher in patients with high HSP 27 than in those with low HSP 27.

**Conclusion:** We found that plasma HSP 27 level can predict cardiac prognosis in patients with chronic heart failure.
Conclusion: Plasma HSP 27 level was associated with severity and cardiac prognosis in patients with CHF secondary to ischemic and dilated cardiomyopathy.

P2750 | BEDSIDE
Use of new echocardiographic parameters to predict acute rejection after heart transplantation. A way to reduce the number of endomyocardial biopsies

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Objective: To analyze the usefulness of conventional and new echocardiographic parameters to exclude acute rejection (AR) after heart transplantation (HT).

Background: AR is a limiting factor of survival after HT. The only validated method to detect AR is endomyocardial biopsy (EB). Recent advances in 2D-strain imaging may allow early detection of AR.

Methods: We included 34 HT performed at our institution between 2010 and 2012. A median of 7 (IQR 6-8) EB and echocardiograms/patient were performed simultaneously along the first year after HT. We analyzed classic echocardiographic parameters and speckle-tracking derived left ventricular (LV) longitudinal (Long), radial and circumferential strain, and Free wall Right ventricular (RV) Long strain.

Results: We analyzed 325 paired EBs and echocardiograms, 62 EBs presented AR (50 1R, 2R and 3 R). Variables independently related to the absence of AR ≥2R were: Free wall RV Long strain −17%, global LV Long strain −15.5% and Lateral Tissue Doppler Imaging (TDI) A: −4.5 cm/s. C-statistic measure to exclude AR ≥2R based on the combination of them was 0.93 (0.86-0.99), with sensitivity 100%, specificity 54.8% and negative predictive value 100%. ROC curves are shown in the figure below.

Conclusions: We propose the combination of three echocardiographic parameters, namely LV and free wall RV global Long-strain and lateral TDI A velocity, to exclude AR after HT. They are simple and reproducible parameters, and in case of external validation its routine measure could be a reliable tool to exclude high degree AR and it may alleviate the burden of repeated EB.

P2751 | BEDSIDE
Immune status in patients with decompensated heart failure: clinical implications

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Purpose: To analyze immune status in patients hospitalized with decompensated chronic heart failure.

To assess contribution of systemic inflammation as one of important pathogenic mechanisms leads patients to hospitalization and immune status towards clinical presentation and 1-year follow-up prognosis.

Methods: Dynamics of a number of haematological and biochemical parameters of peripheral blood were studied. The parameters measured were GFR, hs-CRP, BNP, leukogram, amount of CD 4, CD 25, levels of Ig A,G,M, interleukins 2,6,10, circulating immune complexes, antistreptokinase and antisterptolysine-O and antiphospholipids antibodies, antioxidant plasma activity, and LV function by echocardiography. A total of 52 patients (male -34, female-18) were studied with average age 60.8±3.6 years and EF −35%. The patients were hospitalized with diagnosis of decompensated CHF due to non-valvular causes without any evident signs of inflammation or infection. Patients were assessed at admission, day 4, day of discharge from hospital and 12 months follow-up. Control group included 40 patients without CHF.

Results: See Table 1. Patients with the highest levels of the above mentioned parameters were also characterized by poor clinical indicators, such as longer hospital stay, slower normalization of clinical signs and lab parameters and higher mortality (2 patients died in hospital, 4 during 1-st year after discharge).

Conclusion: Patients with acute decompensation of CHF demonstrated clear immunological signs of chronic infection and/or systemic inflammation. This signs and their severity may have an important prognostic value for both in-patient and follow-up phase of management of patients with decompensated CHF. Some of the immune indicators can be used as an indicator of infection and/or inflammation, altered wall penetrability of colon, severe edema of lower extremities with poor circulation or progression of atherosclerosis.

P2752 | BEDSIDE
Monitoring of intrathoracic impedance can reduce heart failure hospitalization

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Background: A major cause of heart failure (HF) related hospitalizations is fluid accumulation. Recent studies have suggested that intrathoracic impedance (ITI) may be a useful parameter to track daily changes in pulmonary fluid status. OptiVol alert, which is a fluid status algorithm calculated from ITI, can detect impending fluid accumulation at an early stage. However, the clinical utility of this method is not well established. Therefore, we sought to examine whether OptiVol alerts can reduce HF hospitalization.

Methods: We conducted two arms. One was a prospective, multicenter study. HF patients who had been implanted with a high-energy devices with an OptiVol feature were included in this study (OptiVol arm). All patients in OptiVol arm were followed by a wireless remote monitoring system and asked to visit to outpatient clinic after OptiVol alert. Patients took some examinations at enrollment, at OptiVol alert and at HF hospitalization. If we would notify HF sing in outpatient clinic, we intervene along with HF guideline. The other was a retrospective, multicenter study. HF patients who had been implanted with a high-energy devices without an OptiVol feature (Control arm). We compared HF hospitalization rate per year and HF hospitalization free survival rate. And also, we examined the reasons why some patients in OptiVol arm could not avoid HF hospitalization.

Results: One hundred ninety seven patients were enrolled in OptiVol arm and 436 patients were enrolled in Control arm. There was no significant difference in patient characteristics between two arms. HF hospitalization rate per year was significantly lower in OptiVol arm than that in Control arm (0.08±0.39 vs. 0.22±0.61, p<0.001). And HF hospitalization free survival rate was also significantly higher in OptiVol arm than that in Control arm (p<0.05). In OptiVol arm, there were 23 HF hospitalizations. The value of ITI at HF hospitalization was decreased −10% compared with that at baseline (63±4.8 vs 70±7.4, p<0.001). In 15 of 23 HF hospitalizations, OptiVol alerts were notified before HF hospitalization. However, some patients refused visiting hospitals after experience of regular false positive OptiVol alert events, which was one reason. Sometimes, ITI acutely decreased after the false positive OptiVol alert events. However, in these cases, we could not notify acutely decreased ITI, because OptiVol alert did not have function of reminder, which was another reason.

Conclusions: Monitoring of ITI can reduce HF hospitalization. However, OptiVol index and OptiVol alert system would not be enough for clinical use.

Abstract P2751 – Table 1. Results

<table>
<thead>
<tr>
<th>IgA</th>
<th>IgG</th>
<th>CD25</th>
<th>IL-6</th>
<th>CIC</th>
<th>CRP</th>
<th>BNP</th>
<th>EF</th>
<th>Mortality</th>
<th>ASK</th>
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<tr>
<td>D1</td>
<td>2.8±0.4</td>
<td>21.2±2.2</td>
<td>27.3±5.3</td>
<td>35.3±7.7</td>
<td>31.1±6.3</td>
<td>19.4±4.7</td>
<td>112.5±13.1</td>
<td>30.6±2.5</td>
<td>0% 16±2.4</td>
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<tr>
<td>D4</td>
<td>7.2±2.0</td>
<td>34.2±5.1</td>
<td>37.2±5.0</td>
<td>39.8±6.5</td>
<td>16.5±2.9</td>
<td>83.1±4.3</td>
<td>32.3±4.1</td>
<td>2% 161±7</td>
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</tr>
<tr>
<td>DDo</td>
<td>3.5±0.4</td>
<td>22.6±4.3</td>
<td>25.7±4.3</td>
<td>25.3±4.8</td>
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<td>20.1±5.5</td>
<td>42.9±4.9</td>
<td>4% 162±5</td>
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<td>No data</td>
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<td></td>
</tr>
<tr>
<td>Control</td>
<td>2.0±0.4</td>
<td>12.4±5.3</td>
<td>12.7±5.3</td>
<td>2.5±1.1</td>
<td>11.2±1.8</td>
<td>4.6±0.9</td>
<td>25±3</td>
<td>56.3±3.7</td>
<td>0% 45±2.9</td>
</tr>
</tbody>
</table>

CIC, circulating immune complexes; ASK, antistreptokinase.
Response to cardiac resynchronization therapy is improved by combining radial dysynchrony and contractility of the late activated segment

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Background: Speckle tracking echocardiography (STE) has the potential to assess mechanical dysynchrony, and to evaluate viability of the latest activated segment (LAS) by measuring its peak radial strain. The aim of this study was to assess the predictive value of a simple prediction index (Radial Prediction Index - RPI) on the prediction of radial dysynchrony and contractility of LAS.

Methods: Two-dimensional speckle tracking echocardiography was performed in 100 heart failure (HF) patients before undergoing CRT, to assess LV radial dysynchrony (anterosystolic to posterior wall delay <130 msec), and residual myocardial viability (>16% peak radial strain) of the LAS. Concordance between LV lead position (by chest x-ray) and LAS was also evaluated. The RPI was obtained by multiplying radial dysynchrony by peak radial strain of the LAS. Two end-points were considered: 1) >15% reduction in LV end-systolic volume index at 6 months, and 2) combined all-cause mortality and hospitalizations for HF in long-term follow-up.

Results: Three patients were classified as echo responders. RPI was significantly greater in responders than in non-responders (56.5±15.0 vs 14.7±14.1, p<0.0001). After correction for other clinical and echocardiographic predictors, logistic regression analysis revealed that RPI was independently associated with the likelihood of response to CRT (P=0.001). By ROC analysis, a cut-off value of RPI ≥25.6% showed a significantly greater area under the curve than dysynchrony indices alone (p<0.001). This predictive value significantly increased when combined with other markers of LAS position and LAS was present, since prevalence of echo-responders increased to 89% versus 67% when only radial dysynchrony was considered. After a mean follow-up of 19±15 months there were 35 combined events. Cox proportional regression analysis showed that RPI was an independent predictor of worse outcome (log-rank 10.6, P<0.001) after adjusting for other clinical and echocardiographic predictors.

Conclusions: This novel combined index by radial strain echocardiography might be able to predict response to CRT, either in terms of reverse remodeling or long-term prognosis. The discriminatory value of this index in the identification of responders seems to be better than time-delay indexes alone.

Meta analysis echocardiography cardiac resynchronization therapy positive contractile myocardial reserve as a predictor of response

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Purpose: The cardiac resynchronization therapy (CRT) in patients with dilated cardiomyopathy (DCMP) could no response in 40%. Our aim is to determine if the presence of contractile reserve (CR) determined by pharmacology stress test or Late Gadolinium enhancement (LGE) can predict a clinical positive (CIr)- and echocardiography response (Echo-R) to CRT in ischemic and non-ischemic DCMP.

Methods: Condition to investigate was DCMP with ejection fraction (EF) <25%, New York Health Association functional class (FC) ≥ III and QRS >120 ms. The pharmacological measures of RC by echo-CMR, CIr was defined as improvement in at least I FC and Echo-R as increases >5% in EF or reduce>15% in left ventricle end systolic volume (LVESV). Every step was made by two authors independently and the discordances solved by consensus. The searching was made by two authors in PUB med, Chocarane library, EBSCO, Proquest and Lilacs, just for adults humans prospective observational studies. The publication bias was assessed with the funnel plot. The bias risk assessment was done with the chesk liste STROBE. The data was assessed with de Parmar method.

Results: We found 196 articles, 8 were included in the quality analysis. The funnel plot didn’t show published bias. 3 studies included for Clin-R, and 7 for the Echo-R. There was consensus in CRT therapy echo-R between studies. We found that echo CR positive predict Clin-R with an OR 4.42 IC 95% (1.52-12.85). The echo CR predicts Echo-R (lig1) with OR 9. One study reported 38 patients lost, the analysis in the worst scenario showed that Echo-R the OR 8.37 IC 95% (5.58-15.12).

Conclusion: The presence of contractile reserve measure by echocardiography is a parameter important in the detection of good CRT clinical and echocardiography response.

Acute heart failure with preserved or reduced ejection fraction: is it bimodal or overlapping multiple phenotypes?

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Purpose: Whether heart failure with preserved or reduced left ventricular ejection fraction (LVEF) represents distinct or overlapping syndromes and whether they are associated with different outcomes remain unsettled. The different cut offs of ejection fraction used to dichotomize the two syndromes contributed to the confusion surrounding this issue. We sought to characterize further the important clinical features and outcomes of HF in a large hospitalized with acute heart failure study according to a spectrum of LV function strata rather than two dichotomized groups.

Methods: We conducted a prospective registry in 18 hospitals in between October 2009 and December 2010, and followed mortality rates till January 2013. In this sub-study we describe the baseline characteristics and outcomes in this patient population stratified into 4 groups according to LVEF: normal (-50%), mild LV dysfunction (41-50%), moderate LV dysfunction (31-40%) and severe LV dysfunction (<30%).

Results: A total of 2,610 patients were enrolled in this study with mean age (SD) of 61.3 (14.9) and 65.6% were men. Patients with normal LV systolic function and those with severe systolic dysfunction presented two distinct groups. Compared to those with severe systolic dysfunction, patients with normal LVEF were older (64.9 vs. 58.7, p<0.001) with those above 70 years constituted 40% vs 23.3%, more likely treated with diuretics (32.6 vs 23.3%, p<0.001) and have higher body mass index (32.6 vs 28, p<0.001). They also have higher prevalence of hypertension (83.2% vs 63.6%, p<0.001), diabetes (66.9% vs 59.2%, p<0.001), atrial fibrillation (27.7% vs 13.9%, p<0.001) and anemia (33.1% vs 505 Heart failure management
17.9%, p < 0.001). Ischemia and ventricular arrhythmias were less reported in this group (27.3%, and 0.9% vs 56.4% and 5.2%, p < 0.001 respectively). The other two groups with mild and moderate LV systolic dysfunction showed an overlapping spectrum between the normal and severe LV dysfunction groups. All-cause cumulative mortality rates at 30 days, 1 year and 3 years were 8.3%, 19.5% and 24.3%, and were similar in the 4 groups.

**Conclusion:** Classifying acute heart failure patients according to LVEF uncovers two distinct groups with normal LV function and severe dysfunction with a spectrum of phenotypes in between; however, short-term and long-term mortality was similar between these groups. The higher age and comorbidities in the normal LVEF patients may explain the observed similar mortality in the normal and severe LV systolic dysfunction groups.

**P2757 | BEDSIDE**

**Assessment of right ventricular adaptability to load allows prediction of transplant free outcome with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension**

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**Purpose:** Finding predictors of transplant (Tx) free survival with severe pre-capillary pulmonary hypertension and time of Tx listing are main challenges with prolongation in Tx waiting time. Right ventricle (RV) function is highly load-dependent and RV failure (RVF) due to pressure overload is a main cause of death in pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH). Assessment of RV adaptability to load has proven useful for other surgical decisions. Now we assessed its predictive value for outcomes with severe PAH and CTPH aiming to provide new tools for the timing of Tx listing.

**Methods:** At selection and each follow-up control, all Tx candidates with PAH (excluding congenital heart diseases) and CTPH (not suitable for embolus removal) underwent right ventricle (RV) at first evaluation performed in 2006-2012, underwent echocardiography (with tissue Doppler and strain imaging) plus NT-ProBNP and 6 min walk distance (6MWD) measurements. At selection patients (pts) underwent right heart catheterization. For assessment of RV adaptability to load we used a recently validated “load adaptation index” (LAI) based on the relationship between RV load and RV dilatation, taking also RA pressure into account.

Collected data were tested for ability to predict short- (1 year) and mid-term (3 years) RV stability and Tx-free survival.

**Results:** During a 22 to 94 months follow-up, 27 of 102 evaluated pts developed irreversible RVF (16 died before Tx) although all these unstable pts showed similar pulmonary arterial pressure, 6MWD, RV size and RV EF in comparison to pts remaining stable and there were also no differences in medication between these 2 patient groups. However, those with subsequent RVF had initially a lower LAI and RV afterload-corrected peak global longitudinal systolic strain rate (PSSrL), and also higher RV dysynchrony (for all p < 0.01). LAI and afterload-corrected PSSrL stability showed high predictive values for 1 and 3 year freedom from RVF and there were also no differences in medication between these 2 patient groups. However, those with subsequent RVF had initially a lower LAI and RV afterload-corrected peak global longitudinal systolic strain rate (PSSrL), and also higher RV dysynchrony (for all p < 0.01). LAI and afterload-corrected PSSrL stability showed high predictive values for 1 and 3 year freedom from RVF and there were also no differences in medication between these 2 patient groups.

LAI reduction of ≥20% in clinically stable pts with tricuspid regurgitation grade 2 revealed 86% predictive value for short term (>6 months) development of severe RVF. NT-ProBNP, TAPSE and Tei index were initially also more altered in unstable pts but their predictive value for RVF was low.

**Conclusion:** Serial echo follow-up assessment of RV adaptability to load in pts referred for Tx because of severe PAH and CTEPH allow the prediction of RV stability and Tx-free patient survival during the next 1 to 3 years. This can be helpful for timing of Tx listing.

**P2758 | BEDSIDE**

**The mean sleep apnea hypopnea index as a diagnostic criterion for sleep disordered breathing in patients with heart failure**

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**Purpose:** Sleep Disordered Breathing (SDB) is diagnosed in patients with Heart Failure (HF) by calculating the Apnea Hypopnea Index (AHI) typified by a single overnight Polysomnography (PSG) study. Repeated PSG studies over 2-4 nights have, however, shown that the AHI may vary in type and severity in these patients.

We hypothesized that due to alveolar fluid changes in HF patients, the AHI would be ≤5% and ≤24.3% ± 31.5m in NYHA IV patients. There was no significant difference between 6MWT values in each NYHA class, and thus determine the objectivity of the NYHA criteria in assessing functional class in heart failure patients.

**Methodology:** The search terms “Comparison of NYHA to 6MWT”, “NYHA and 6MWT” and “heart failure and 6MWT” were entered into the PubMed database, yielding 328 papers. 48 studies comparing 6MWT in each NYHA class were included. 280 papers were excluded, with 81 studies describing 6MWT values in at least 100 NYHA class in heart failure patients and 199 studies failing to compare NYHA to 6MWT. We then obtained the mean and standard deviation of 6MWT for each NYHA class for each paper and compared them across each NYHA class.

**Results:** The 48 studies consisted of 28 from Europe, 13 from the USA, 5 from Asia and 2 from South America. A total of 11014 patients (7502 males, mean age 59.3±10.6 years old) were studied. Mean 6MWT was 446.1±123.1m in NYHA I patients, 401.5±95.0m in NYHA II patients, 328.3±80.7m in NYHA III patients and 232.0±31.5m in NYHA IV patients. There was no significant difference between 6MWT values in each NYHA class, with much overlap in 6MWT distances among all 4 groups (see Fig. 1).

**Conclusion:** The NYHA criteria has an element of subjectivity that may be influenced by multiple factors. More objective measures such as the 6MWT may be included in studies to provide better definition of the patient’s functional status.

**HEART FAILURE NEWS**

**P2759 | BEDSIDE**

**Assessment of the subjectivity of the NYHA classification: use of the 6 minute walk test**

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**Purpose:** The New York Heart Association (NYHA) functional class status has been used in the vast majority of heart failure studies as well as in many guidelines. However, the NYHA class status includes an element of subjectivity. We aim to review the literature on all studies done with correlation between 6 Minute Walk Test Distance (6MWT) and New York Heart Association (NYHA) functional class and thus determine the objectivity of the NYHA criteria in assessing functional class in heart failure patients.

**Methodology:** The search terms “Comparison of NYHA to 6MWT”, “NYHA and 6MWT” and “heart failure and 6MWT” were entered into the PubMed database, yielding 328 papers. 48 studies comparing 6MWT in each NYHA class were included. 280 papers were excluded, with 81 studies describing 6MWT values in 5199 NYHA class and 199 studies failing to compare NYHA to 6MWT. We then obtained the mean and standard deviation of 6MWT for each NYHA class for each paper and compared them across each NYHA class.

**Results:** The 48 studies consisted of 28 from Europe, 13 from the USA, 5 from Asia and 2 from South America. A total of 11014 patients (7502 males, mean age 59.3±10.6 years old) were studied. Mean 6MWT was 446.1±123.1m in NYHA I patients, 401.5±95.0m in NYHA II patients, 328.3±80.7m in NYHA III patients and 232.0±31.5m in NYHA IV patients. There was no significant difference between 6MWT values in each NYHA class, with much overlap in 6MWT distances among all 4 groups (see Fig. 1).

**Conclusion:** The NYHA criteria has an element of subjectivity that may be influenced by multiple factors. More objective measures such as the 6MWT may be included in studies to provide better definition of the patient’s functional status.
years old with normal LV contraction and no signs or history of symptomatic heart failure, ischemic heart diseases, atrial fibrillation, stroke, or cognitive dysfunction. For the estimation of LV diastolic function, E/E' measured by tissue Doppler echocardiography offers an indicator of the severity of LV diastolic dysfunction, reflecting both diastolic LV stiffness and diastolic LV filling pressure. The volume of cerebral WMLs was quantified on brain MRI.

**Results:** Mean age was 69.3±3.4 years, E/E' ratio 11.8±3.5, and the volume of cerebral WMLs 6.4±1.7 mL. Linear regression analysis showed the positive association between E/E' ratio and the volume of WMLs (r=0.377, p=0.0009). Then, we re-estimated the association between E/E' ratio and the volume of WMLs, using another multivariate linear regression analysis adjusted for confounding factors such as age, hypertension, diabetes, and sex. As a result, a direct association between E/E' ratio and the volume of WMLs was confirmed (p=0.0057).

**Conclusions:** This investigation identified a direct association between LV diastolic dysfunction and cerebral WMLs. Further investigation is needed to clarify the mechanisms.

**P2762 | BEDSIDE**

Abnormal fibrin clot structure in chronic heart failure

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**Background and purpose:** Chronic Heart Failure (CHF) is an overwhelming healthcare burden with poor clinical outcomes and high mortality rates. One reason for these poor outcomes is the abnormal haemostatic balance leading to stroke, venous thrombosis, bleeding and sudden death. Abnormal fibrin clot properties in CHF may explain the phenomenon of the prothrombotic and increased haemorrhagic state in these patients. Coagulation and clot lysis can be assessed by Thrombelastography (TEG), fibrinolysis and turbidimetric assays.

**Methods:** Whole blood and plasma from 15 CHF patients and 15 healthy controls were analysed by TEG, fibrinolysis and turbidimetric assay. Data were compared by t-test.

**Results:** Using TEG, no statistically significant differences were seen in whole blood from CHF subjects compared to controls: mean R-time (10.2 minutes vs. 8.5 minutes, p=0.414) and K-time (1.9 minutes vs. 2.1 minutes, p=0.8), α-angle (64.0° vs. 60.2°, p=0.3) Maximum Amplitude (66.7mm vs. 66.9mm, p=0.9) and LY60 (2.4% vs. 3.9%, p=0.3). Turbimetric analysis revealed increased absorbance of light through fibrin clot in CHF patients (0.6 vs 0.5, p<0.003). Fibrinolysis assay showed no difference in time to lyse 50% of clot (16.3 mins vs. 18.4 minutes, p=0.3) but a significantly steeper slope of fibrin clot lysis in CHF subjects (2.5 vs 1.8, p=0.01).

**Conclusions:** Thicker fibrin clots are formed in CHF (as demonstrated by increased absorbance), followed by an increased rate of fibrin clot lysis in CHF. TEG shows no evidence of abnormal clot kinetics in patients with CHF. This may potentially explain the increased haemorrhagic risk associated with CHF patients on warfarin seen in recent trials.

**P2764 | BEDSIDE**

Dilated inferior vena cava at admission is a prognostic factor for cardiovascular events in heart failure patients with preserved ejection fraction

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**Purpose:** Heart failure (HF) with preserved ejection fraction (HFpEF) has been increasing in recent years, with poor prognosis. However, few studies report on the risk factors for readmission for HFpEF. Hence, we investigated the risk factors for readmission for HF, particularly those with preserved EF (pEF).

**Method:** We retrospectively studied the medical records of 416 first-onset HF patients admitted to our hospital from 2009–2013. In this study, 171 of whom were classified as pEF. The step endpoint was readmission due to heart failure. HF-pEF was defined as LVEF >50% and according to ESC guidelines. Data regarding medical history, vital signs, electrocardiogram, chest X-rays, blood tests, and echocardiograms were collected and compared between patients with pEF and those with reduced EF (rEF). The chi-square test, Student’s t-test, and Kaplan–Meier survival curves were used to compare variables between the patients, as appropriate. Univariate analysis was performed on all items, and those with statistical significance were selected. Multivariate analysis was performed on variables with a P<0.05 using the stepwise multiple regression approach (step-up method).

**Results:** Of the 171 pEF patients, 49 reached the endpoint over 1 year. Multivariate analysis revealed high blood urea nitrogen (BUN) level at admission [hazard ratio (HR): 1.045], dilated inferior vena cava (IVC) at admission (HR: 1.088), medical history of old myocardial infarction (HR: 3.033), and old cerebral infarction (HR: 3.006) as independent risk factors for readmission. In contrast, 64 of 243 rEF patients reached the endpoint. Risk factors for rEF patient readmission were low systolic blood pressure at admission (HR: 0.977), high blood urea nitrogen level (HR: 1.049), low albumin level (HR: 0.307) at discharge, and absence of beta-blocker use (HR: 0.498). We calculated the Kaplan–Meier survival curves and compared them using log-rank tests. Significant differences were shown for all factors.

**Conclusion:** Our study suggests dilated inferior vena cava at admission was a predictor of readmission for HFpEF patients.

**P2765 | BENCH**

Increased volume load due to stimulation of renal beta1-adrenoceptors by beta1-adrenoceptor antibodies contributes to the progression of dilated immune-myoangiopathy

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**Conclusion:** This investigation identified a direct association between LV diastolic dysfunction and cerebral WMLs. Further investigation is needed to clarify the mechanisms.
hypertensive phenotype may, at least in part, rely on a antibody-induced stimulation of renal P1-ARs.

Methods: N=40 Lewis rats were monthly immunized with a P1-ECII/GST fusion protein, n=20 NaCl (0.9%)-injected rats served as controls. Antibody titers & cardiac function were followed every 3 months by ELISA & by echocardiography. In addition, every month we analyzed plasma renin activity, drinking behavior, serum electrolytes, and 24-h urine samples. Glomerular filtration rate (GFR) and renal plasma flow (RPF) were assessed invasively before harvesting the kidneys for further histological and molecular analysis.

Results: Chronic stimulation of the kidney by anti-P1-ECII abs results in an initial increase in renin mRNA levels, indicating activation of P1-ARs in the membrane of renin producing granular cells within the juxtaglomerular apparatus. In the course of our study renin mRNA levels decreased. These findings fit well with the observed transient increase in plasma renin activity and the increase in GFR in immunized versus control rats suggesting renin-mediated hyper-filtration. In addition, P1-ECII antibody-induced stimulation of P1-ARs in the distal tubules resulted in a significant increase in sodium and chloride reabsorption. Physiologically this initiates a decrease in aldosterone secretion and, hence, negatively affects potassium secretion. This cascade further enhances sodium and (passive) water reabsorption, thus by volume overload contributing to the initial hypertensive phenotype.

In conclusion we show here that stimulating anti-P1-ECII appear in fact to be able to modulate function, in particular during P1-ARs localized (a) on renin-producing macula densa cells, and (b) on distal tubular cells, which might –by volume overload– indirectly accelerate switching of the hypertensive to the DCM phenotype.

P2766 | BEDSIDE
Impaired gas diffusion correlates with right heart-pulmonary circulation uncoupling and ventilation inefficiency during exercise in heart failure

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An altered gas diffusing capacity for carbon monoxide (DLCO) is a marker of lung capillary injury that bears relevant clinical and prognostic information in heart failure (HF) patients. It is unknown whether right heart-pulmonary circulation (RH-PC) uncoupling abnormalities in gas diffusion are linked and may become synergetic in causing exercise limitation and ventilation inefficiency.

Methods: 12 HFpEF patients (mean age 64±11; male 75%; NYHA II-III; mean left ventricular (LV) ejection fraction 34±11%) underwent DLCO measurements by single breath technique and maximal cardiopulmonary exercise testing (CPET, tilt-ergometer, personalized ramp protocol) combined with Echo-Doppler assessment. The RH-PC coupling was assessed by monitoring the ratio of tricuspid annular peak systolic excursion (TAPSE)/pulmonary arterial pressure (PASP) and the end-diastolic changes during exercise.

Results: Patients exhibited an abnormal gas diffusion (mean DLCO 17±4.1 ml/min/mmHg) elevated PASP (mean 43.5±9.4 mmHg) and depressed TAPSE (mean 15.9±4.2 mm) along with significant functional limitation (mean peak VO2 11.6±2.9 ml/kg/min) and ventilatory inefficiency (mean VE/VO2 slope 35.7±7.7 and mean end-tidal of CO2 mean 31.6±5.8 mmHg). The figure below show the correlations existing between DLCO and other ventilatory or echo-derived parameters.

Figure 1. Correlations.

Conclusions: Our findings suggest a link between the RV-PH uncoupling with gas diffusion abnormalities suggesting that interventions aimed at targeting the right heart and functional performance have to combine a modulatory effect on the alveolar-capillary gas diffusion capacity.

P2767 | BENCH
Endothelial protein tyrosine phosphatase 1b deficiency reduces both endothelial and cardiac dysfunction of in a mouse model of heart failure

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Purpose: Chronic heart failure (CHF) is associated with an endothelial dysfunction, and especially a decrease in nitric oxide (NO) production, however the direct link between endothelial dysfunction and aggravation of CHF is not established. We reported previously a new potent therapeutic approach of CHF, based on inhibition of protein tyrosine phosphatase 1B (PTP1B), which both increases NO production (via restored PI3K/Akt/eNOS signaling) and reduces adverse Left Ventricular (LV) remodeling and LV dysfunction. To address the direct link between endothelial protection and reduction of CHF, we evaluate the cardiac and vascular consequences of endothelial PTP1B deficiency (endoPTP1B−/−) in a mouse model of CHF.

Methods: EndoPTP1B−/− mice, developed by crossing LOX-P PTP1B mice with mice expressing CRE under the control of the endothelial promoter Tie2, or wild-type (WT) mice were subjected to left coronary artery ligation or sham surgery, and the development of CHF was assessed by echocardiography at 2 weeks, and 1, 2 and 3 months, and endothelial function at 3 months.

Results: WT CHF mice showed a markedly impaired flow-mediated dilation of isolated mesenteric arteries (sham: 40±4%; CHF: 5±5%; p<0.001), which was improved in endoPTP1B−/− mice (30±5%; p<0.001 vs. WT CHF). These responses were reduced by a NO-synthase inhibitor, showing the implication of NO. In WT, CHF increased LV diameters and decreased LV fractional shortening (at 3 months: sham: 49±12; CHF: 12±1%; p<0.001) while these parameters were improved in endoPTP1B−/− mice (20±12%; p<0.01). LV pressure-volume curves showed that endoPTP1B−/− mice with CHF had reduced LV end-systolic (at 3 months: 25±1; 2±1%; CHF WT: 14.9±1.9%, p<0.05) and increased end-diastolic pressure-volume relationships (sham: 2.1±0.9; CHF WT: 4.9±0.7%, p<0.05) demonstrating impaired systolic and diastolic dysfunction, respectively, which were both improved in endoPTP1B−/− mice (endo: 20±2; 2±2.3%; p<0.05; end-diastolic: 2.3±0.9%, p<0.05). Histological analysis showed cardiomyocytes hypertrophy and increased collagen density in WT CHF mice, which were reduced in endoPTP1B−/− mice, at identical infarct size. These beneficial cardio-vascular effects were associated with a significant increase in survival (CHF WT: 44%, CHF endoPTP1B−/− 87%, p<0.001).

Conclusions: Thus, in this mouse model of CHF, endoPTP1B deficiency not only improved an endothelial function, but also of cardiac function, adverse LV remodeling and survival. These results provide a direct demonstration of the beneficial effect of endothelial protection in the treatment of CHF.

P2768 | BEDSIDE
Prevalence and long-term prognosis of functional mitral regurgitation in Asian symptomatic heart failure in recent era of cardiovascular clinical practice


Purpose: Previous studies performed in Western countries in 1980s to 1990s demonstrated that functional MR (FMR) was a common and critical condition in HF patients. However, sophisticated patients care improved the prognosis of HF and the epidemiology of HF in Asia is different from that in Western countries. In the present study, we aimed to clarify the prevalence and prognosis of FMR in Asian HF patients in contemporary era.

Methods: With a single hospital-based cohort in the Shinken Database 2004-2011, which comprised all new patients (n=17,517) who visited our institute, we followed symptomatic HF patients (NYHA ≥II).

Results: A total of 1,701 patients were included: 104 FMR patients [who had moderate – severe FMR]: 907 non-FMR patients [who had none or mild MR]. FMR patients had lower rates of hypertension, but had higher rates of DCM, AF, and NYHA III/IV. FMR patients had higher BNP level and lower LVEF. Use of cardiovascular drugs was more common in patients with FMR patients. Kaplan-Meier curves revealed that the incidences of all-cause death, cardiovascular death, and HF admission were significantly higher in FMR patients. The adjusted multivariate Cox regression analysis showed that significant functional MR was associated with higher incidences of all cause death (HR 2.179, 95% CI 1.266-3.751, p<0.005), cardiovascular death (HR 2.371, 95% CI 1.157-4.858, p=0.018), and HF admission (HR 1.819, 95% CI 1.133-2.920, p=0.013). In subanalysis, there was no significant difference in the mortality of FMR patients between with and without surgical MR intervention.

Conclusion: FMR was common in Asian symptomatic HF patients and was
still associated with adverse outcomes in contemporary era. Establishing optimal therapeutic strategies for FMR is strongly warranted.

P2769 | SPOTLIGHT
The HDL proteome analyses of chronic heart failure reveals new insights in disease related HDL function
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Background: High density lipoproteins (HDL) exerts endothelial-protective effects via stimulation of endothelial cell (EC) NO production. An abnormality in the intracellular iron metabolism is a key phenomenon in patients with chronic heart failure (CHF). To test the hypothesis that HDL particles are remodelled under the CHF conditions we characterized the proteome of HDL of healthy controls compared with CHF patients with impaired endothelial-protective function

Material and method: HDL was isolated from five healthy controls (HDLcontrol) and 5 patients with CHF-NHYA-Ilb (HDLNHYA-Illb). First, EC were incubated with HDL and phosphorylation of eNOS-Ser177, eNOS-Thr495, PKC-ßII-Ser411 and p70S6K-Ser411 was evaluated. Second, in-depth proteome characterisation of HDL particle was performed by online strong cation exchange fractionation with reverse phase liquid chromatography (2D LC-MS).

Results: Incubation of EC with HDL-NHYA-Ilb triggered a lower stimulation of phosphorylation at eNOS-Ser177 and a higher phosphorylation at eNOS-Thr495 whereas no changes to HDL-heathy. The 2D-nanoLC-MS/MS shotgun proteome analysis of HDL particles identified 494 distinct proteins, whereas 118 proteins were commonly found in more than 50% of each group indicating a high variability among the HDL particles and sample types. Several proteins varied between NHYA Illb patients compared to healthy controls. Those proteins may exert a specific biological function related to the pathophysiology of chronic heart failure.

Conclusion: These results demonstrate that HDL-function is impaired in CHF and may provide a molecular basis for a better understanding of proteome complexity and their functional diversity in HDL-NHYA-Illb.

P2770 | BENCH
Cardiomyocytes and myocyte cells contain the molecular system of intracellular iron metabolism and respond to environmental iron changes in in vitro conditions
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Background: There are premises that iron plays a critical role in the functioning of cardiomyocytes and skeletal myocyte cells. The presence of the molecular system of proteins involved in intracellular iron metabolism in these cells is anticipated.

Methods: H9C2 rat adult cardiomyocytes and L6G8SC5 (L6) rat myocyte cells were cultured for 24 hours: a) during the optimal conditions (optimal oxygen partial concentration in the medium (iron chelatation - 50 μM DFO); c) during the increased iron concentration in the medium (added ammonium ferric citrate 100 μM or 200 μM). We analysed the expression of mRNAs of the following genes: HIF-1α (hypoxia and iron depletion indicator), ferritin heavy and light chain (FTL and FTH), myoglobin (MB; oxygen storage), ferritin heavy chain in the medium (iron chelatation - 50 μM or 100 μM deferoxamine, DFO); c) during the increased iron concentration in the medium (added ammonium ferric citrate 100 μM or 200 μM). We analysed the expression of mRNAs of the following genes: HIF-1α (hypoxia and iron depletion indicator), ferritin heavy and light chain (FTL and FTH), myoglobin (MB; oxygen storage), ferroportin (FPN1; cellular iron exporter), transferrin receptor type 1 (TR1; cellular iron uptake), hepclin (HAMP; iron metabolism regulator) using qPCR, and the level of respective proteins using Western Blot.

Results: H9C2 cells (cardiomyocytes) exposed to gradually reduced iron concentrations in the medium demonstrated an increased expression of HIF-1α as compared to cells cultured in control conditions (r < 0.001, p < 0.0001), and a decrease in the expression of FTL (r = 0.91, p < 0.0001), FTH (r = 0.96, p < 0.0001), MB (r = -0.75, p < 0.005) and HAMP (r = -0.75, p < 0.05). All these changes confirmed the induction of depleted iron status in examined cells. As a consequence, the expression of TR1 (r = 0.70, p < 0.05) was increased, reflecting a facilitating entrance of iron to the cells. The inverse changes occurred in H9C2 cells exposed to high (100 μM or 200 μM) iron concentration in comparison to cells cultured in control conditions. The same pattern of changes in gene expression was observed in L6 cells (myocyte cells), and there was a strong correlation between analogous genes in both cell lines (genes r > 0.90, p < 0.0001). The WB analysis of proteins encoded by aforementioned genes revealed the same pattern of changes as that seen in the gene expression profile.

Conclusions: Both rat cardiomyocytes and myocyte cells contain the set of genes involved in the intracellular iron metabolism, and both types of investigated cells respond to iron concentrations and respond to environmental iron changes in gene and protein profiles reflect the physiological adaptive mechanism aiming to counteract the unfavourable iron status occurring in the environment and affecting the cultured cells.

P2771 | BEDSIDE
Relationship of serum erythropoietin level to short-term clinical outcome in patients with acute decompensated heart failure

Purpose: High serum erythropoietin (EPO) level has been reported to be associated with adverse events in chronic heart failure (CHF). However, its prognostic significance in patients with acute decompensated HF (ADHF) remains unknown.

Methods: We examined 280 consecutive ADHF patients who admitted to our institution between January 2013 and December 2013 from prospective registry. Patients who had acute coronary syndrome, without accessible EPO level at admission and/or failed to be followed-up over 60 days were excluded. Finally, 173 patients were divided into two groups according to higher serum EPO level (above 34 μl/mI, the median lower serum EPO level (below 34 μl/mI) at admission. Adverse events were defined as re-exacerbation of HF and death within 60 days after admission.

Results: Adverse events were occurred in 19 patients (11%). Higher serum EPO group had significantly higher incidence of adverse events compared with lower serum EPO group (18.2% vs 3.5%, P=0.001). Patients with higher serum EPO level had higher hemoglobin level and higher serum creatinine, plasma brain natriuretic peptide (BNP) levels and increased iron status. Oxygen saturation was significantly different between the two groups in terms of age, gender, blood pressure, etiology of ADHF, cardiovascular medications, left ventricular ejection fraction, serum troponin-T, C-reactive protein (CRP) levels on admission, and early management for HF. Multivariate logistic regression analyses showed that higher serum EPO level (odds ratio 5.0, 95% CI 1.5-22.6, P<0.005) was an independent determinant for adverse events within 60 days after admission, among variables including age, gender, blood pressure, serum creatinine, hemoglobin, and plasma BNP levels on admission.

Conclusions: Higher serum EPO level might be a predictor for short-term adverse events in patients with ADHF.

HEART FAILURE MATTERS

P2773 | BEDSIDE
Congestive heart failure with concomitant tachyarrhythmia: predictors for tachycardiomyopathy
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Introduction: Differential diagnosis of tachycardiomyopathy (TC) from other cardiomyopathies remains challenging in patients presenting with new onset congestive heart failure (CHF) and concomitant tachyarrhythmia. Given the benign prognosis of TC defining clinical associates that predict complete resolution of left ventricular systolic dysfunction (LVSD) after rhythm control are utterly needed. Therefore, the aim of this study was to determine the factors that predict complete resolution of LVSD in patients with new onset CHF and concomitant tachyarrhythmia.

Methods: Using an institutional echo database we screened for patients with new onset LVSD (LV ejection fraction (LVEF) <40%) in the presence of tachyarrhythmia. Multivariate logistic regression analyses showed that higher serum EPO level (odds ratio 5.0, 95% CI 1.5-22.6, P<0.005) was an independent determinant for adverse events within 60 days after admission, among variables including age, gender, blood pressure, serum creatinine, hemoglobin, and plasma BNP levels on admission.

Conclusions: Higher serum EPO level might be a predictor for short-term adverse events in patients with ADHF.
Resting heart rate and real life treatment modality in outpatients with left ventricular systolic dysfunction (REALITY HF) study

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Purpose: Resting heart rate (HR) is referred as a target of therapy and important predictor of prognosis in chronic heart failure (HF) and HR reduction is associated with improved outcomes in randomized clinical trials. However, less is known about resting HR and related treatment modalities in real life practice. Resting HR and treatment modality in outpatients with Left ventricular Systolic Dysfunction (REALITY HF) study was a multicenter, prospective, observational, national registry designed to evaluate resting HR and the effects of current treatment modalities in real life clinical practice.

Methods: REALITY HF enrolled 1054 patients (mean age 61.1±12 years, 76% male, from 16 centers) admitted to the outpatient clinic with the diagnosis of chronic HF and LV EF <40%. Clinical characteristics, HR and medications were noted (enrollment phase). 487 patients with sinus rhythm and HR ≥70 bpm were included in further 4-month follow-up (FU) program (V0). Adjustment of HF medication was left to physician discretion. Changes in HR and medications were reevaluated at 1-month (V1) and 4-month (V2) FU. Health-related quality of life (QoL) was assessed by Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score (OSS) scale at V0 and at V2.

Results: During enrollment, 93% of patients were receiving evidence-based HF medication and 82% were on ≥2 drug therapy including ACEI (61.7%) or ARB (12.7%), beta blocker (BB) (81%), aldosterone blocker (35.4%) or digoxin (12.6%). 794 patients (75%) were in sinus rhythm, in which mean HR was 76±14 bpm and 68% of these patients had a resting HR ≥70 bpm. Mean HR was lower in patients receiving BB (75.8±13 vs 80.4±16 bpm, p=0.001), however, 66% of those had a resting HR >70 bpm. In patients participating 4-m FU, BB therapy was uptitrated in 43.7% of patients at V0 and 12.9% at V1, ivabradine was initiated in 7.6% of patients at V0 and 11.5% at V1, and digoxin was initiated or adjusted in 3.9% at V0 and in 1.8% at V1 by the clinicians. Mean HR significantly reduced from 83.6±12 bpm at V0 to 78.6±13 bpm at V1 (p<0.001) and further decreased to 73.0±11 bpm at V2 (p<0.001). Proportion of patients achieving a resting HR <70 bpm was 21.7% at V1 (p<0.001) and 39.9% at V2 (p<0.001). KCCQ OSS significantly increased from 59.7±23 at V0 to 73.1±18 at V2 (p<0.001). Also, proportion of patients with NYHA I increased from 24.4% at V0 to 29.3% at V1 and 39.3% at V2.

Conclusions: In real life clinical practice, treatment modalities targeting HR in patients with chronic HF significantly reduce resting HR and reduction in resting HR is associated with improved health related QoL.

Resting heart rate and real life treatment capacity in heart failure

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Purpose: Resting heart rate (HR) is referred as a target of therapy and important predictor of prognosis in chronic heart failure (HF) and HR reduction is associated with improved outcomes in randomized clinical trials. However, less is known about resting HR and related treatment modalities in real life practice. Resting HR and treatment modality in outpatients with Left ventricular Systolic Dysfunction (REALITY HF) study was a multicenter, prospective, observational, national registry designed to evaluate resting HR and the effects of current treatment modalities in real life clinical practice.

Methods: REALITY HF enrolled 1054 patients (mean age 61.1±12 years, 76% male, from 16 centers) admitted to the outpatient clinic with the diagnosis of chronic HF and LV EF <40%. Clinical characteristics, HR and medications were noted (enrollment phase). 487 patients with sinus rhythm and HR ≥70 bpm were included in further 4-month follow-up (FU) program (V0). Adjustment of HF medication was left to physician discretion. Changes in HR and medications were reevaluated at 1-month (V1) and 4-month (V2) FU. Health-related quality of life (QoL) was assessed by Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score (OSS) scale at V0 and at V2.

Results: During enrollment, 93% of patients were receiving evidence-based HF medication and 82% were on ≥2 drug therapy including ACEI (61.7%) or ARB (12.7%), beta blocker (BB) (81%), aldosterone blocker (35.4%) or digoxin (12.6%). 794 patients (75%) were in sinus rhythm, in which mean HR was 76±14 bpm and 68% of these patients had a resting HR ≥70 bpm. Mean HR was lower in patients receiving BB (75.8±13 vs 80.4±16 bpm, p=0.001), however, 66% of those had a resting HR >70 bpm. In patients participating 4-m FU, BB therapy was uptitrated in 43.7% of patients at V0 and 12.9% at V1, ivabradine was initiated in 7.6% of patients at V0 and 11.5% at V1, and digoxin was initiated or adjusted in 3.9% at V0 and in 1.8% at V1 by the clinicians. Mean HR significantly reduced from 83.6±12 bpm at V0 to 78.6±13 bpm at V1 (p<0.001) and further decreased to 73.0±11 bpm at V2 (p<0.001). Proportion of patients achieving a resting HR <70 bpm was 21.7% at V1 (p<0.001) and 39.9% at V2 (p<0.001). KCCQ OSS significantly increased from 59.7±23 at V0 to 73.1±18 at V2 (p<0.001). Also, proportion of patients with NYHA I increased from 24.4% at V0 to 29.3% at V1 and 39.3% at V2.

Conclusions: In real life clinical practice, treatment modalities targeting HR in patients with chronic HF significantly reduce resting HR and reduction in resting HR is associated with improved health related QoL.
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Predictors of exercise-induced pulmonary hypertension in patients with preserved left ventricular ejection fraction

Purpose: Exercise-induced pulmonary hypertension (EIPH) is uncommon in patients with preserved LVEF. However, there is limited data on predictors of EIPH in these subjects, and its clinical implications are unclear. Our study attempted to analyze EIPH predictors in patients with preserved LVEF and to investigate its association with exercise capacity.

Methods: Overall 1,404 patients referred for exercise stress echocardiography were included. EIPH was defined as PASP > 35 mmHg at exercise. Patients with positive exercise stress echocardiography, significant valvular heart disease, atrial fibrillation, or LVEF lower than 50% were excluded.

Results: EIPH did develop in 447 patients (32%). Those subjects were older, more often male, and had higher BMI and shorter exercise duration. In the multivariable analysis, independent predictors of EIPH were age (p < 0.001), RVSP at rest (p < 0.001), E/e' ratio at exercise (p = 0.022), and maximal SBP at exercise (p = 0.014). However, this multivariable model did not show any significant differences of exercise capacity (exercise duration or metabolic equivalents) between the two groups.

Conclusion: In this large cross-sectional study, exercise-induced pulmonary hypertension in patients with preserved LVEF is independently associated with age, RVSP at rest, E/e' ratio and maximal SBP at exercise.

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Clinical significance of hypocapnia in patients with stable chronic heart failure
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The clinical significance of hypocapnia in stable chronic heart failure (CHF) has not been fully investigated so far. Accordingly, we sought to clarify the significance in patients with stable CHF. We prospectively performed arterial blood gas analysis in 123 patients with CHF (NYHA functional class III or IV) and left ventricular ejection fraction (LVEF) ≤ 50%. The patients were divided into the 2 groups according to the presence (group A, n = 17) or absence (group B, n = 106) of hypocapnia (partial pressure of arterial carbon dioxide (PaCO2) < 35 mmHg). Group A had an older age (71.1 ± 7.6 years vs. 64.2 ± 12.7 years, p = 0.04), a higher arterial pH (7.45 ± 0.03 vs. 7.41 ± 0.03, p < 0.001), a lower HCO3- (22.8 ± 1.5 mmol/L vs. 23.6 ± 2.4 mmol/L, p < 0.001), a higher brain natriuretic peptide (BNP) level (439 ± 486 pg/ml vs. 194 ± 274 pg/ml, p = 0.001), a higher central apnea index (8.2 ± 12.2 vs. 2.7 ± 6.6, p = 0.005), and a higher cardiac washout rate of 123I-MIBG (r = -0.31, p = 0.001) and central apnea index (r = -0.24, p = 0.011). A logistic multivariate analysis revealed that log BNP was significantly associated with hypocapnia (odds ratio 4.7, 95% confidence interval 1.5 - 14.2, p = 0.006), and a multiple regression analysis showed that cardiac washout rate of 123I-MIBG were significantly associated with PaCO2 (beta = 0.31, p = 0.001). In conclusion, this study suggests that hypocapnia in stable CHF is associated with its severity and resultant activated cardiac sympathetic nervous system, both of which can cause hyperventilation and thereby contribute to the occurrence of central sleep apnea.

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Haemodynamic response to exercise one year after heart transplantation
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Purpose: Heart transplantation (HT) is the ultimate therapy for end-stage heart failure. Despite that the normal magnitudes of haemodynamic parameters are well defined in healthy individuals, there is scarce knowledge on their magnitudes after HT, especially with regards to the response to exercise. The impact of the age dependent differences, seen in healthy subjects, furthermore needs evaluation after HT. We haemodynamically characterized our patients at rest and during exercise one year after HT, to observe the haemodynamic response to exercise and investigate potential age dependent differences in the exercise response.

Methods: We analyzed 32 adults (31% women; mean age 51 yrs), evaluated with right heart catheterization, at our lab, at rest and during exercise one year after HT performed 1988-2010. Men exercised at 50 W and women at 30 W. The most common diagnosis was dilated cardiomyopathy (68%). 12 patients were ≤ 50 and 20 were > 50 yrs of age. Paired t- or Wilcoxon Signed rank tests were performed when analyzing the response to exercise. T- or Mann-Whitney Rank Sum tests were performed when comparing the groups. P < 0.05 was considered significant.

Results: Resting total pulmonary vascular resistance (TPVR) was 50 yrs. In exercise patients:50yrs increased (p < 0.05) mean pulmonary artery pressure (MPAP) by 14.8 ± 1.6 mmHg (114%), pulmonary artery wedge pressure (PAWP) by 12.1 ± 1.4 mmHg (91%), transpulmonary gradient (TPG) by 2.8 ± 3.3 mmHg (43%), mean right atrial pressure (MPRA) by 8.8 ± 5.8 mmHg (463%), cardiac output (CO) by 5.8 ± 3.4 L/min (89%) and TPVR by 0.2 ± 0.4 WU (10%), whereas PVR decreased (p < 0.003) by 0.4 ± 0.3 WU (27%). Exercise in patients ≥ 50 yrs increased (p < 0.008) MPAP by 19.6 ± 6.2 mmHg (122%), PAWP by 15.3 ± 5.9 mmHg (228%), TPG by 4.3 ± 2.8 mmHg (33%), MPRA by 10.6 ± 3.5 mmHg (44%), CO by 5.1 ± 1.6 L/min 1 (89%) and TPVR by 0.5 ± 0.8 WU (12%). Moreover, a great number of patients did not meet the criteria for CRT due to improve and additional criteria for best selection are needed. Left ventricular mechanical dyssynchrony (LVMd) assessed by phase analysis of gated myocardial perfusion imaging (MPI) may be a useful tool for predicting response to CRT.

Discussion: There was no age dependent difference in exercise response one year after HT. Although the response to exercise was adequate, there was an aggragated increase in MPAP, MPRA and, in particular, PAWP. This response was true both for patients aged ≤ 50 yrs and > 50 yrs. As a result of the exaggerated increase in PAWP to exercise “normalized” after HT, whereas the TPVR response remained deranged. This suggests that TPVR may be more adequate than PVR for evaluations post-HT.
Atorvastatin treatment mobilizes endothelial progenitor cells in early stages of ischemic heart failure

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Purpose: Patients with heart failure (HF) manifest endothelial dysfunction. Circulating endothelial progenitor cells (EPC) contribute to reendothelialization and repair of damaged endothelium in HF. Statins with anti-inflammatory and pleiotropic properties can restore endothelial function in HF. Aim of the present study was to examine the effects of different doses of atorvastatin treatment and clinical status, on mobilization of EPC and endothelial function in patients with ischemic HF.

Methods: We studied the effect of 4 weeks atorvastatin treatment in 23 subjects with ischemic HF at New York Heart Association (NYHA) functional class II and III. The study was carried out on two separate arms, one with atorvastatin 40mg/d and one with atorvastatin 10mg/d (randomized, double-blind, crossover design). Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Serum levels of tumor necrosis factor alpha (TNFα) were measured by ELISA. The number of circulating CD34+/CD133+/KDR(+) EPCs were evaluated by flow cytometry.

Results: From the study population, 15 subjects were categorized as NYHA II and 8 subjects as NYHA III. Compared to baseline, treatment with 40 mg/d of atorvastatin improved FMD (3.16±2.98% vs. 6.05±2.45%, p=0.001), TNFα levels [1.08 (0.79-1.35) pg/ml vs. 0.85 (0.68-1.24) pg/ml, p=0.01] and circulating EPC [362 (209-456) cells/ml vs. 175 (143-232) cells/ml, p=0.002]. Similarly, compared to baseline, treatment with atorvastatin 10mg/d also improved FMD (3.24±2.12% vs. 4.20±2.09%, p=0.08), TNFα [1.11 (0.73-1.37) pg/ml vs. 0.99 (0.64-1.12) pg/ml, p=0.01] and EPC [201 (151-309) cells/ml vs. 169 (115-228) cells/ml, p=0.01]. The increase in EPC (p=0.02) and FMD (p=0.001) was greater with the dose of 40 mg/d. Moreover, in the 40 mg/day atorvastatin treatment group we found an association between baseline FMD and increased EPC numbers (r=0.48, p=0.03). Importantly, in the 40 mg/day atorvastatin treatment group, the increase in EPC was higher in NYHA II subjects compared to NYHA III subjects (217±142 cells/ml vs. 60±150 cells/ml, p=0.03).

Conclusions: In ischemic HF subjects, both high and low dose atorvastatin treatment mobilizes EPC and improves endothelial function with a parallel anti-inflammatory effect. This improvement is more pronounced in subjects with better clinical status and better functional endothelium. These findings shed some light on the pleiotropic effects of statins in patients with ischemic HF.

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